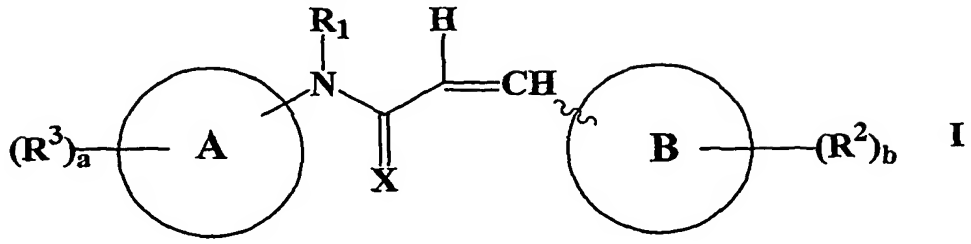
CLAIMS

What is claimed is:

1. A compound of formula I:



I

wherein:

ring A and ring B are independently selected from the group consisting of aryl and heteroaryl, provided that ring A is other than pyridyl, quinazolyl or naphthyridyl;

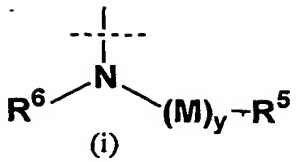
X is O or S;

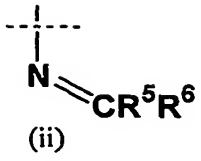
R^1 is independently selected from the group consisting of $-R^4$, $-SO_2(C_1-C_6)$alkyl, $-C(=O)R^4$, $-C(=O)OR^4$, $-C(=O)O(C_1-C_6)$alkylenearyl, $-OR^4$, $-(C_2-C_6)$alkynyl, $-(C_3-C_6)$heteroalkenyl, $-(C_2-C_6)$alkylene-OR^4, substituted aryl, unsubstituted aryl, substituted heteroaryl, unsubstituted heteroaryl, substituted aryl(C_1-C_3)alkyl, unsubstituted aryl(C_1-C_3)alkyl, substituted heteroaryl(C_1-C_3)alkyl and unsubstituted heteroaryl(C_1-C_3)alkyl;

each R^2 is independently selected from $-OR^4$, halogen, $-C\equiv N$, $-CO_2R^4$, $-C(=O)NR^4{}_2$, $-C(=NR^4)NR^4{}_2$, $-O(C_1-C_3)$alkylene-CO_2R^4, $-(C_2-C_6)-OR^4$, phosphonato, $-NR^4{}_2$, $-NHC(=O)(C_1-C_6)$alkyl, sulfamyl, carbamyl, $-OC(=O)(C_1-C_3)$alkyl, $-O(C_2-C_6)-N((C_1-C_6)\text{alkyl})_2$, $-S(C_1-C_3)$alkyl, $-S(=O)(C_1-C_3)$alkyl, and $-SO_2(C_1-C_3)$alkyl;

b is 1, 2, 3, 4, or 5;

R^3 is independently selected from halogen, $-(C_1-C_6)$alkyl, $-OR^4$, $-C\equiv N$, $-C(=NR^4)NR^4{}_2$, $-O(C_1-C_3)$alkylene-CO_2R^4, $-(C_1-C_6)-OR^4$, nitro, phosphonato, $-NHC(=O)(C_1-C_6)$alkyl, sulfamyl, $-OC(=O)(C_1-C_3)$alkyl, $-O(C_2-C_6)-N((C_1-C_6)\text{alkyl})_2$ and (i) or (ii) below:


(i)


(ii)

wherein:

each M is a bivalent connecting group independently selected from the group consisting of –(C_1-C_6)alkylene–, –$(CH_2)_d$-V-$(CH_2)_e$–, –$(CH_2)_f$-W-$(CH_2)_g$– and –Z–;

each y is independently selected from the group consisting of 0 and 1;

each V is independently selected from the group consisting of arylene, heteroarylene, -C(=O)-, -C(=O)(C_1-C_6)perfluoroalkylene, –C(=O)–, –C(=S)–, –S(=O)–, –SO_2–, –C(=O)NR^4–, –C(=S)NR^4– and –SO_2NR^4–;

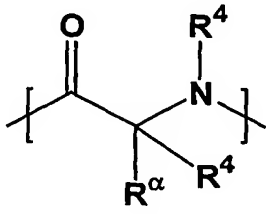
each W is independently selected from the group consisting of –NR^4–, –O– and -S–;

each d is independently selected from the group consisting of 0, 1 and 2;

each e is independently selected from the group consisting of 0, 1 and 2;

each f is independently selected from the group consisting of 1, 2 and 3;

each g is independently selected from the group consisting of 0, 1 and 2;

-Z- is 
;

wherein the absolute stereochemistry of –Z– is S or R, or a mixture of S and R;

each R^{α} is independently selected from the group consisting of -H, -(C_1-C_6)alkyl, -$(CH_2)_3$-NH-C(NH_2)(=NH), -$CH_2C(=O)NH_2$, -CH_2COOH, -CH_2SH, -$(CH_2)_2C(=O)$-NH_2, -$(CH_2)_2COOH$, -CH_2-(2-imidazolyl), -$(CH_2)_4$-NH_2, -$(CH_2)_2$-S-CH_3, phenyl, -CH_2-phenyl, -CH_2-OH, -CH(OH)-CH_3, -CH_2-(3-indolyl), -CH_2-(4-hydroxyphenyl); and includes compounds wherein R^{α} and R^4 combine to form a 5-, 6- or 7-membered heterocyclic or carbocyclic ring;

a is 1, 2 or 3;

R^4 is independently selected from the group consisting of –H, -(C_1-C_6)alkyl, substituted -(C_1-C_6)alkyl, -(C_2-C_6)alkenyl, substituted -(C_2-C_6)alkenyl and heteroalkyl, wherein two R^4 groups may together form a heterocycle;

each R^5 is independently selected from the group consisting of -R^4, unsubstituted aryl, substituted aryl, substituted heterocyclic, unsubstituted heterocyclic, -CO_2R^4, -$C(=O)NR^4_2$, -$C(=NH)$-NR^4_2, -(C_1-C_6)perfluoroalkyl, -CF_2Cl, -$P(=O)(OR^4)_2$, -$OP(=O)(OR^4)_2$, -$CR^4R^7R^8$ and a monovalent peptidyl moiety with a molecular weight of less than 1000; provided that when y is 0 and R^5 is –CO_2R^4, then R^4 is not –H;

each R^6 is independently selected from the group consisting of –H, -(C_1-C_6)alkyl, and aryl(C_1-C_3)alkyl,

each R^7 is independently selected from the group consisting of –H, -(C_1-C_6)alkyl, –C(=O)R^8, -OR^4, -SR^4, -$OC(=O)(CH_2)_2CO_2R^6$, guanidino, NR^4_2, -$NR^4_3{}^+$, -$N^+(CH_2CH_2OR^5)_3$, halogen, phenyl, substituted phenyl, heterocyclyl, and substituted heterocyclyl; and

each R^8 is independently selected from the group consisting of R^{α}, halogen, -NR^4_2 and heterocycles containing two nitrogen atoms;

wherein the substituents for the substituted aryl and substituted heterocyclic groups comprising or included within Ar, R^1, R^5 R^6, R^7 and R^{α} are independently selected from the group consisting of halogen, -(C_1-C_6)alkyl, -(C_1-C_6)alkoxy, -NO_2, -C≡N, -$C(=O)O$(C_1-C_3)alkyl, -OR^4, -(C_2-C_6)-OR^4, phosphonato, -NR^4_2, -NHC(=O)(C_1-C_6)alkyl, sulfamyl, carbamyl, -$OC(=O)$(C_1-C_3)alkyl, -O(C_2-C_6)-N((C_1-C_6)alkyl)$_2$ and -(C_1-C_3)perfluoroalkyl;

~~~~ indicates a single bond, whereby the compounds of formula I may be in either the E or the Z conformation;

provided that:

when A is phenyl, R^3 is other than 3,4,5-tri-OR^4;

when R^2 is 4-methoxy, R^3 is other than 4-methoxy;

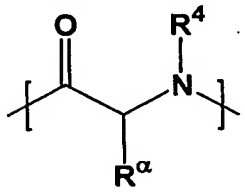
when B is phenyl, R^2 is other than 2,3-di-OR^4 and 3,4-di-OR^4; and

when R^3 is halogen, R^2 is not chlorine, bromine or iodine;

or a salt of such a compound.

2. A compound according to claim 1,

wherein –Z– is:



;

wherein the absolute stereochemistry of –Z– is either S or R; and

each R^α is independently selected from the group consisting of -H, $-CH_3$, $-(CH_2)_3-NH-C(NH_2)(=NH)$, $-CH_2C(=O)NH_2$, $-CH_2COOH$, $-CH_2SH$, $-(CH_2)_2C(=O)-NH_2$, $-(CH_2)_2COOH$, $-CH_2$-(2-imidazolyl), $-CH(CH_3)-CH_2CH_3$, $-CH_2CH(CH_3)_2$, $-(CH_2)_4-NH_2$, $-(CH_2)_2-S-CH_3$, phenyl, CH_2-phenyl, $-CH_2-OH$, $-CH(OH)-CH_3$, $-CH_2$-(3-indolyl), $-CH_2$-(4-hydroxyphenyl), $-CH(CH_3)_2$ and $-CH_2CH_3$; and includes compounds wherein R^α and R^4 combine to form a 5-, 6- or 7-membered heterocyclic ring.

3. A compound according to claim 2 wherein the compound is selected from the group consisting of:

(*E*)-*N*-(4-methoxy-3-nitrophenyl)-3-(3,4,5-trimethoxyphenyl)-2-propenamide;

(*E*)-*N*-(4-methoxy-3-aminophenyl)-3-(3,4,5-trimethoxyphenyl)-2-propenamide;
~~~~

(*E*)-*N*-(4-methoxy-3-nitrophenyl)-3-(2,3,4,5,6-pentafluorophenyl)-2-propenamide;

(*E*)-*N*-(4-bromophenyl)-3-(3-methoxy-4-fluorophenyl)-2-propenamide;

(*E*)-*N*-(4-bromophenyl)-3-(3-cyano-4-fluorophenyl)-2-propenamide;

(*E*)-*N*-(4-bromophenyl)-3-(3-carboxy-4-fluorophenyl)-2-propenamide;

(*E*)-*N*-(4-methoxy-3-nitrophenyl)-3-(3-fluoro-4-nitrophenyl)-2-propenamide;

(*E*)-*N*-(4-bromophenyl)-3-(2,4-difluorophenyl)-2-propenamide;

(*E*)-*N*-(4-methoxy-3-aminophenyl)-3-(3-fluoro-4-aminophenyl)-2-propenamide;

and salts thereof.

4. A compound according to claim 2 wherein

each V is independently selected from the group consisting of –C(=O)–, –C(=S)–, –S(=O)–, $-SO_2-$, –C(=O)NR^4–, –C(=S)NR^4– and $-SO_2NR^4-$.

5. A compound according to claim 4 wherein

R^2 is independently selected from $-OR^4$, -C≡N, $-CO_2R^4$, $-C(=O)NR^4{}_2$, $-C(=NR^4)NR^4{}_2$, $-O(C_1\text{-}C_3)$alkylene-CO_2R^4, $-(C_2\text{-}C_6)$-OR^4, phosphonato, $-NR^4{}_2$, $-NHC(=O)(C_1\text{-}C_6)$alkyl, sulfamyl, carbamyl, $-OC(=O)(C_1\text{-}C_3)$alkyl, $-O(C_2\text{-}C_6)$-$N((C_1\text{-}C_6)\text{alkyl})_2$, $-S(C_1\text{-}C_3)$alkyl, $-S(=O)(C_1\text{-}C_3)$alkyl, and $-SO_2(C_1\text{-}C_3)$alkyl;

b is 1, 2 or 3; and

each R^7 is independently selected from the group consisting of –H, $-(C_1\text{-}C_6)$alkyl and $-(C_1\text{-}C_6)$acyl.

6 A compound according to claim 4 wherein the compound is (*E*)-*N*-(4-methoxy-3-trifluoroacetamidophenyl)-3-(2,4,6-trimethoxyphenyl)-2-propenamide or a salt thereof.

7. A compound according to claim 5, wherein each R^5 is independently selected from the group consisting of $-R^4$, unsubstituted aryl,

substituted aryl, substituted heterocyclic, unsubstituted heterocyclic, $-CO_2R^4$, $-C(=O)NR^4{}_2$, $-C(=NH)-NR^4{}_2$, and a monovalent peptidyl moiety with a molecular weight of less than 1000; provided that when y is 0 and R^5 is $-CO_2R^4$, then R^4 is not –H; and

wherein the substituents for the substituted aryl and substituted heterocyclic groups comprising or included within Ar, R^1, R^5 and R^α are independently selected from the group consisting of halogen, $-(C_1-C_6)$alkyl, $-(C_1-C_6)$alkoxy, $-NO_2$, $-C\equiv N$, $-C(=O)O(C_1-C_3)$alkyl, $-OR^4$, $-(C_2-C_6)-OR^4$, phosphonato, $-NR^4{}_2$, $-NHC(=O)(C_1-C_6)$alkyl, sulfamyl, carbamyl, $-OC(=O)(C_1-C_3)$alkyl, $-O(C_2-C_6)-N((C_1-C_6)\text{alkyl})_2$ and $-(C_1-C_3)$perfluoroalkyl; or a salt of such a compound.

8. A compound according to claim 7, wherein:

one R^3 substituent, designated R^{3p}, is positioned in a substitution orientation relative to the $-N(R^1)-C(=X)-CH=CH-$(B)$-R^2$ moiety of Formula I which is closest to the planar angle formed by a para substituent in a six-membered aromatic ring and forms a planar angle with the $-N(R^1)-C(=X)-CH=CH-$(B)$-R^2$ moiety of between about 135° and about 180°;

R^{3p} is selected from the group consisting of halogen, $-(C_1-C_6)$alkyl, $-(C_1-C_6)$alkoxy, $-C\equiv N$, $-C(=O)NR^4{}_2$, $-C(=NR^4)NR^4{}_2$, $-O(C_1-C_3)$alkylene-CO_2R^4, $-OR^4$, $-(C_2-C_6)-OR^4$, phosphonato, $-NR^4{}_2$, $-NHC(=O)(C_1-C_6)$alkyl, sulfamyl, $-OC(=O)(C_1-C_3)$alkyl, $-O(C_2-C_6)-N((C_1-C_6)\text{alkyl})_2$ and $-(C_1-C_3)$perfluoroalkyl;

wherein ring A, ring B, X, M, d, e, f, g, V, W, Z, R^1, R^2, R^4, R^5, R^6, R^7, a, b, y, R^α, and any remaining R^3 substituents are as defined in claim 1;

or a salt of such a compound.

9. A compound according to claim 8 wherein the compound is selected from the group consisting of:

(*E*)-*N*-(4-methoxyphenyl)-3-(2,4,6-trimethoxyphenyl)-2-propenamide;

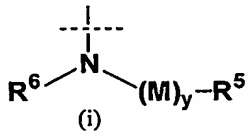
(*E*)-*N*-(4-methoxyphenyl)-3-(2,6-dimethoxyphenyl)-2-propenamide;

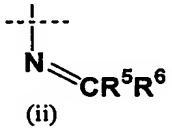
(*E*)-*N*-(3-hydoxy-4-methoxyphenyl)-3-(2,4,6-trimethoxyphenyl)-2-propenamide; and salts of such compounds.

10. A compound according to claim 8 wherein:

at least one R^3 substituent, designated R^{3m} is positioned in a substitution orientation relative to the $-N(R^1)-C(=X)-CH=CH-$(B)$-R^2$ moiety of Formula I which is closest to the planar angle formed by a meta substituent in a 6-membered aromatic ring and forms a planar angle with the $-N(R^1)-C(=X)-CH=CH-$(B)$-R^2$ moiety of between about 90° and about 145°;

each R^{3m} is selected from the group consisting of nitro and (i) and (ii) below:


(i)


(ii)

ring A, ring B, M, d, e, f, g, V, W, Z, R^1, R^2, R^{3p}, R^4, R^5, R^6, R^7, a, b, y, R^α, and the remaining R^3 substituents are as defined in claim 7;

or a salt of such a compound.

11. A compound according to Claim 10 wherein:

ring A is phenyl; and

ring B, and M, d, e, f, g, V, W, Z, R^1, R^2, R^3, R^{3m}, R^{3p}, R^4, R^5, R^6, R^7, a, b, y and R^α are as defined in claim 9; or a salt of such a compound.

12. A compound according to Claim 10 wherein:

ring B is phenyl; and

ring A, and M, d, e, f, g, V, W, Z, R^1, R^2, R^3, R^{3m}, R^{3p}, R^4, R^5, R^6, R^7, a, b, y and R^α are as defined in claim 9; or a salt of such a compound.

13. A compound according to Claim 12 wherein:

ring A is phenyl; and

M, d, e, f, g, V, W, Z, R^1, R^2, R^3, R^{3m}, R^{3p}, R^4, R^5, R^6, R^7, a, b, y and R^α are as defined in claim 11;

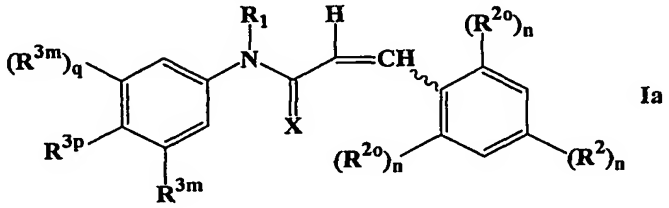
or a salt of such a compound.

14. A compound according to claim 13 wherein at least one R^2 substituent, designated R^{2o} is positioned at an ortho- or 1,2- substitution orientation on ring B relative to the ~CH=CH-C(=X)-N(R^1)-(A)-(R^3)$_a$ moiety of formula I; and

X, M, d, e, f, g, V, W, Z, R^1, R^2, R^3, R^{3m}, R^{3p}, R^4, R^5, R^6, R^7, a, b, y and R^α are as defined in claim 12;

or a salt of such a compound.

15. A compound according to claim 14 of formula Ia:



Ia

wherein:

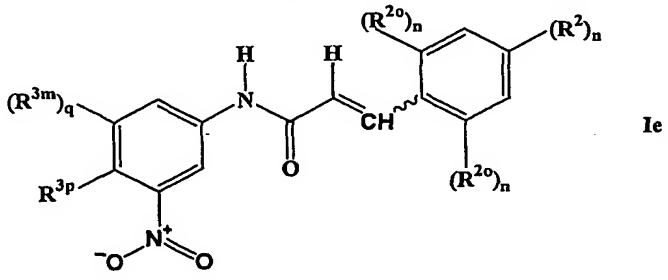
q is 0 or 1

each n is independently selected from 0 and 1; wherein the sum of n is selected from 1, 2 and 3; and

~~~, X, R^1, R^2, R^{2o}, R^{3m}, R^{3p}, and n are as defined in claim 14;

or a salt of such a compound.

16. A compound according to claim 15 of formula Ie



Ie
~~~

wherein:

q, n, R^2, R^{2o}, R^{3m} and R^{3p} are defined as in claim 15;

or a salt of such a compound.

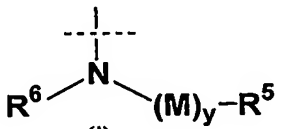
17. A compound according to claim 16 of formula Ie wherein the compound is selected from the group consisting of:

(*E*)-*N*-(4-methoxy-3-nitrophenyl)-3-(2,4,6-trimethoxyphenyl)-2-propenamide; and salts of such a compound.

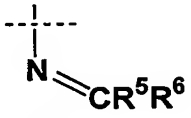
18. A compound according to claim 16

wherein:

each R^{3m} is independently selected from the group consisting of (i) and (ii) below:



(i)



(ii)

R^{3p} is selected from the group consisting of halogen, -(C_1-C_6)alkyl, -(C_1-C_6)alkoxy, -C≡N, -C(=O)NR^4_2, -C(=NR^4)NR^4_2, –O(C_1-C_3)alkylene-CO_2R^4, -OR^4, -(C_2-C_6)-OR^4, phosphonato, -NR^4_2, -NHC(=O)(C_1-C_6)alkyl, sulfamyl, -OC(=O)(C_1-C_3)alkyl, -O(C_2-C_6)-N((C_1-C_6)alkyl)$_2$ and -(C_1-C_3)perfluoroalkyl;

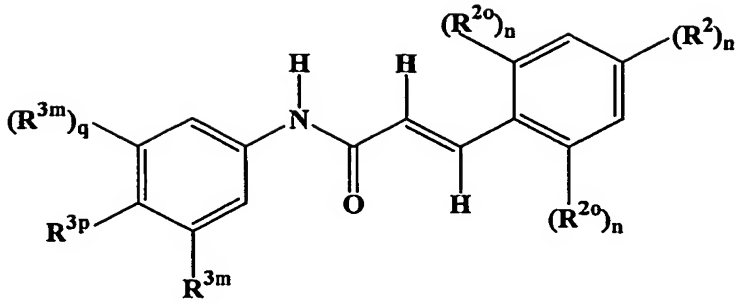
each R^{2o} is independently selected from the group consisting of -(C_1-C_6)alkoxy, -NR^4_2, -OC(=O)(C_1-C_3)alkyl and -O(C_2-C_6)-N((C_1-C_6)alkyl)$_2$;

R^2 is selected from the group consisting of halogen, -(C_1-C_6)alkyl, -(C_1-C_6)alkoxy, -NR^4_2, -C≡N, -CO_2R^4, -C(=O)NR^4_2, -C(=NR^4)NR^4_2, and -(C_1-C_3)perfluoroalkyl;

n is 0 or 1; and

X, M, d, e, f, g, V, W, Z, R^1, R^3, R^4, R^5, R^6, R^7, a, b, n, y and R^α are as defined in claim 16; or a salt of such a compound.

19. A compound according to claim 18 of formula Ib



Ib

wherein:

R^1 is –H;

X is O; and

the conformation of the olefin double bond is *E*, and

R^2, R^{2o}, R^{3m}, R^{3p}, q and n are defined as in claim 18;

or a salt of such a compound.

20. A compound according to claim 19 wherein:

R^{2o} is -(C_1-C_6)alkoxy;

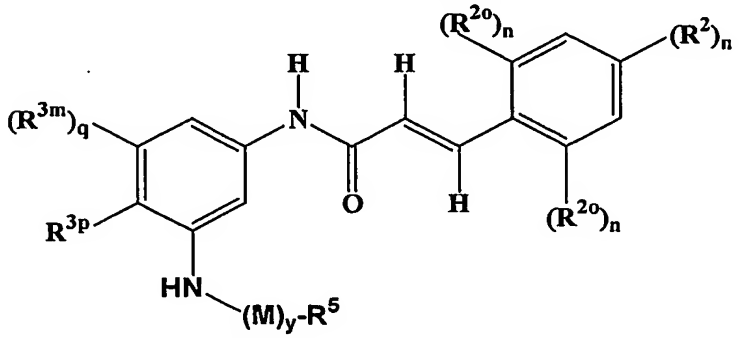
R^2 is selected from the group consisting of halogen, -(C_1-C_6)alkyl, -(C_1-C_6)alkoxy and –NR^4_2;

n is 0 or 1; and

q is 0 or 1;

or a salt of such a compound.

21. A compound according to claim 20 of the formula Ic:



Ic

wherein R^2, R^{2o}, R^{3m}, R^{3p} , q, n, M, y and R^5 are as defined in claim 20;

or a salt of such a compound.

22. A compound according to claim 21, wherein the compound is selected from the group consisting of:

(*E*)-*N*-(4-methoxy-3-aminophenyl)-3-(2,4,6-trimethoxyphenyl)-2-propenamide;

2-[({5-[(2E)-3-(2,4,6-trimethoxyphenyl)prop-2-enoylamino]-2-methoxyphenyl}amino)sulfonyl]acetic acid;

2-(*N*-{5-[(2E)-3-(2,4,6-trimethoxyphenyl)prop-2-enoylamino]-2-methoxyphenyl}carbamoyl)acetic acid;

(2E)-*N*-[3-(amidinoamino)-4-methoxyphenyl]-3-(2,4,6-trimethoxyphenyl)prop-2-enamide;

2-({5-[(2E)-3-(2,4,6-trimethoxyphenyl)prop-2-enoylamino]-2-methoxyphenyl}amino)acetic acid;

(2E)-*N*-{3-[(3,5-dinitrophenyl)carbonylamino]-4-methoxyphenyl}-3-(2,4,6-trimethoxyphenyl)prop-2-enamide;

(2E)-*N*-{3-[(3,5-diaminophenyl)carbonylamino]-4-methoxyphenyl}-3-(2,4,6-trimethoxyphenyl)prop-2-enamide;

(2E)-*N*-[3-(2-chloroacetylamino)-4-methoxyphenyl]-3-(2,4,6-trimethoxyphenyl)prop-2-enamide;

(2E)-*N*-{4-methoxy-3-[2-(4-methylpiperazinyl)acetylamino]-phenyl}-3-(2,4,6-trimethoxyphenyl)prop-2-enamide;

(2E)-*N*-[4-methoxy-3-(phenylcarbonylamino)phenyl]-3-(2,4,6-trimethoxyphenyl)prop-2-enamide;

(2E)-*N*-{4-methoxy-3-[(4-nitrophenyl)carbonylamino]phenyl}-3-(2,4,6-trimethoxyphenyl)prop-2-enamide;

(2E)-*N*-{3-[(4-aminophenyl)carbonylamino]-4-methoxyphenyl}-3-(2,4,6-trimethoxyphenyl)prop-2-enamide;

(2E)-*N*-{3-[(1Z)-1-aza-2-(4-nitrophenyl)vinyl]-4-methoxyphenyl}-3-(2,4,6-trimethoxyphenyl)prop-2-enamide;

(2E)-*N*-[3-((2R)-2,6-diaminohexanoylamino)-4-methoxyphenyl]-3-(2,4,6-trimethoxyphenyl)prop-2-enamide;

(2E)-*N*-[3-((2R)-2-amino-3-hydroxypropanoylamino)-4-methoxyphenyl]-3-(2,4,6-trimethoxyphenyl)prop-2-enamide;

(2E)-*N*-[3-((2S)-2-amino-3-hydroxypropanoylamino)-4-methoxy-phenyl]-3-(2,4,6-trimethoxyphenyl)prop-2-enamide;

(2E)-*N*-[3-(aminocarbonylamino)-4-methoxyphenyl]-3-(2,4,6-trimethoxyphenyl)prop-2-enamide;

(2E)-*N*-[4-methoxy-3-(methylamino)phenyl]-3-(2,4,6-trimethoxy-phenyl)prop-2-enamide;

(2E)-*N*-[3-(acetylamino)-4-methoxyphenyl]-3-(2,4,6-trimethoxy-phenyl)prop-2-enamide;

(2E)-*N*-(3-{[(2,4-dinitrophenyl)sulfonyl]amino}-4-methoxyphenyl)-3-(2,4,6-trimethoxyphenyl)prop-2-enamide;

(2E)-*N*-(3-{[(2,4-diaminophenyl)sulfonyl]amino}-4-methoxy-phenyl)-3-(2,4,6-trimethoxyphenyl)prop-2-enamide;

(2E)-*N*-{3-[2-(dimethylamino)acetylamino]-4-methoxyphenyl}-3-(2,4,6-trimethoxyphenyl)prop-2-enamide;

2-({5-[(2E)-3-(2,4,6-trimethoxyphenyl)prop-2-enoylamino]-2-methoxyphenyl}amino)propanoic acid;

(2E)-*N*-(4-methoxy-3-{[4-(4-methylpiperazinyl)phenyl]-carbonyl-amino}phenyl)-3-(2,4,6-trimethoxyphenyl)prop-2-enamide;

(2E)-*N*-[3-(2-hydroxyacetylamino)-4-methoxyphenyl]-3-(2,4,6-trimethoxyphenyl)prop-2-enamide;

(2E)-*N*-[4-methoxy-3-(2-pyridylacetylamino)phenyl]-3-(2,4,6-trimethoxyphenyl)prop-2-enamide;

(*N*-{5-[(2E)-3-(2,4,6-trimethoxyphenyl)prop-2-enoylamino]-2-methoxyphenyl}carbamoyl)methyl acetate;

(2E)-*N*-[3-(2-hydroxypropanoylamino)-4-methoxyphenyl]-3-(2,4,6-trimethoxyphenyl)prop-2-enamide;

(2E)-*N*-{4-methoxy-3-[2-(triethylammonium)acetylamino]-phenyl}-3-(2,4,6-trimethoxyphenyl)prop-2-enamide;

(2E)-*N*-(4-methoxy-3-{2-[tris(2-hydroxyethyl)ammonium]-acetylamino}phenyl)-3-(2,4,6-trimethoxyphenyl)prop-2-enamide;

(2E)-*N*-[3-(2-hydroxy-2-methylpropanoylamino)-4-methoxyphenyl]-3-(2,4,6-trimethoxyphenyl)prop-2-enamide;

1-(*N*-{5-[(2E)-3-(2,4,6-trimethoxyphenyl)prop-2-enoylamino]-2-methoxyphenyl}carbamoyl)-isopropyl acetate;

(2E)-*N*-[4-methoxy-3-(2,2,2-trifluoroacetylamino)phenyl]-3-(2,4,6-trimethoxyphenyl)prop-2-enamide;

(2E)-*N*-(4-methoxy-3-{[(trifluoromethyl)sulfonyl]-amino}phenyl)-3-(2,4,6-trimethoxyphenyl)prop-2-enamide;

3-(*N*-{5-[(2E)-3-(2,4,6-trimethoxyphenyl)prop-2-enoylamino]-2-methoxyphenyl}carbamoyl)propanoic acid;

3-(*N*-{5-[(2E)-3-(2,4,6-trimethoxyphenyl)prop-2-enoylamino]-2-methoxyphenyl}carbamoyl)propanoyl chloride;

3-{[(*N*-{5-[(2E)-3-(2,4,6-trimethoxyphenyl)prop-2-enoylamino]-2-methoxyphenyl}carbamoyl)methyl]oxycarbonyl}propanoic acid;

4-(*N*-{5-[(2E)-3-(2,4,6-trimethoxyphenyl)prop-2-enoylamino]-2-methoxyphenyl}carbamoyl)butanoic acid;

(2E)-*N*-{4-methoxy-3-[2-(phosphonooxy)acetylamino]phenyl}-3-(2,4,6-trimethoxyphenyl)prop-2-enamide, disodium salt;

4-({5-[(2E)-3-(2,4,6-trimethoxyphenyl)prop-2-enoylamino]-2-methoxyphenyl}amino)butanoic acid;

3-({5-[(2E)-3-(2,4,6-trimethoxyphenyl)prop-2-enoylamino]-2-methoxyphenyl}amino)propanoic acid;

(2E)-*N*-[4-methoxy-3-(methoxycarbonylamino)phenyl]-3-(2,4,6-trimethoxyphenyl)prop-2-enamide;

(2E)-*N*-(4-methoxy-3-{[(4-methoxyphenyl)sulfonyl]-amino}phenyl)-3-(2,4,6-trimethoxyphenyl)prop-2-enamide;

(*N*-{5-[(2E)-3-(2,4,6-trimethoxyphenyl)prop-2-enoylamino]-2-methoxyphenyl}carbamoyl)ethyl acetate;

methyl 3-(*N*-{5-[(2E)-3-(2,4,6-trimethoxyphenyl)prop-2-enoylamino]-2-methoxyphenyl}carbamoyl)propanoate;

ethyl 2-(*N*-{5-[(2E)-3-(2,4,6-trimethoxyphenyl)prop-2-enoylamino]-2-methoxyphenyl}carbamoyl)acetate;

(2E)-*N*-[4-methoxy-3-(2,2,3,3,3-pentafluoropropanoylamino)-phenyl]-3-(2,4,6-trimethoxyphenyl)prop-2-enamide;

methyl 2-(*N*-{5-[(2E)-3-(2,4,6-trimethoxyphenyl)prop-2-enoyl-amino]-2-methoxyphenyl}carbamoyl)-2,2-difluoroacetate;

3-(*N*-{5-[(2E)-3-(2,4,6-trimethoxyphenyl)prop-2-enoylamino]-2-methoxyphenyl}carbamoyl)-2,2,3,3-tetrafluoropropanoic acid;

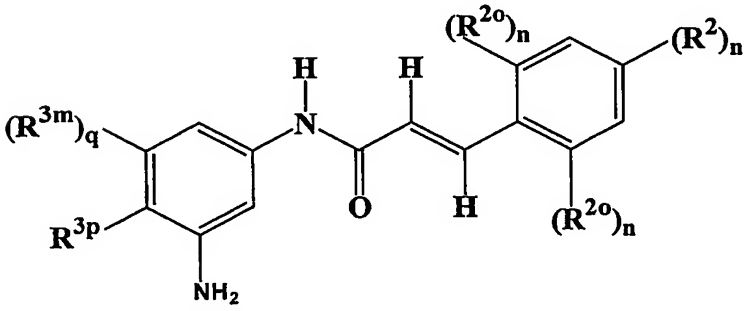
(2E)-*N*-[3-(2-aminoacetylamino)-4-methoxyphenyl]-3-(2,4,6-trimethoxyphenyl)prop-2-enamide;

2-(*N*-{5-[(2E)-3-(2,4,6-trimethoxyphenyl)prop-2-enoylamino]-2-methoxyphenyl}carbamoyl)-2,2-difluoroacetic acid;

(2E)-*N*-{3-[2-(dimethylamino)-2,2-difluoroacetylamino]-4-methoxyphenyl}-3-(2,4,6-trimethoxyphenyl)prop-2-enamide; and

salts of such compounds.

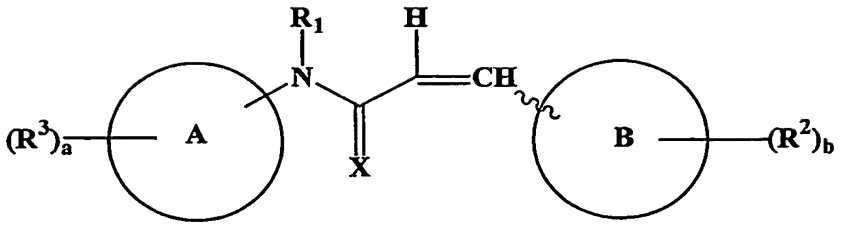
23. A compound according to claim 21 of the formula Id:



Id

wherein R^2, R^{2o}, R^{3m}, R^{3p}, n, and q are defined as in claim 21,or a salt of such a compound..

24. A process for preparing a compound according to claim 7, which compound has the formula I,



I

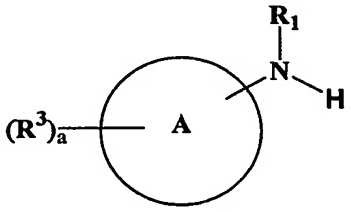
wherein:

the olefin double bond is in the *E* conformation; and

R^1, R^2, R^3, a, b, X, A and B are as defined in claim 7;

comprising:

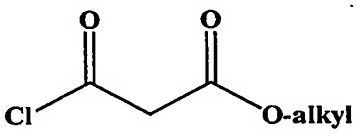
(1) coupling a compound of formula II:



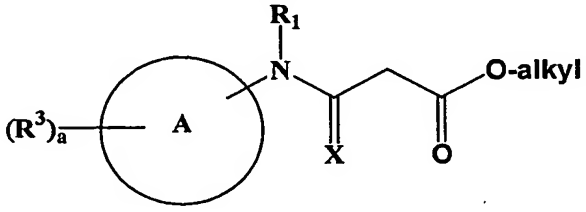
II

wherein A, R^1, R^3, and a are defined as in claim 7;

with an alkyl ester of malonic acid chloride:

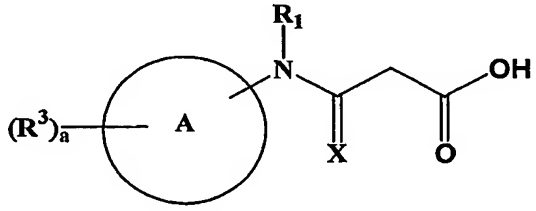


to yield a carboxylic ester compound of formula III:



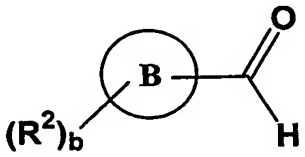
III

(2) hydrolyzing the carboxylic ester compound of formula III to form a carboxylic acid compound of formula IV:



IV

(3) coupling of the carboxylic acid compound of formula IV with an aromatic aldehyde of formula V:



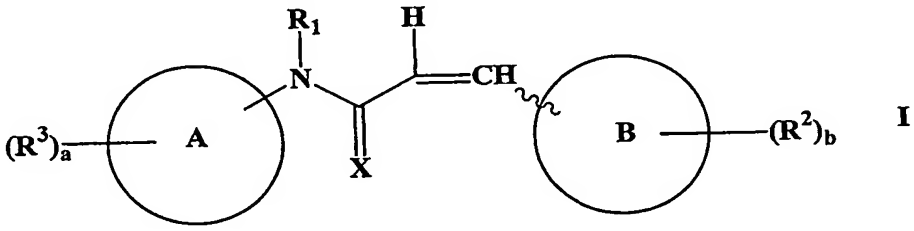
V

wherein R^2, B and b are defined as in claim 7;

in glacial acetic acid at elevated temperature to form a compound of formula I;

or a salt of such a compound.

25. A process for preparing a compound according to claim 7, which compound has the formula I,



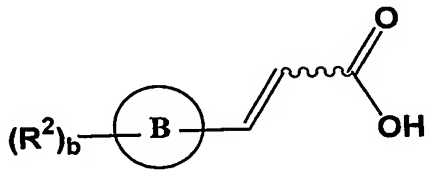
I

wherein:

R^1, R^2, R^3, a, b, X, A and B are as defined in claim 7;

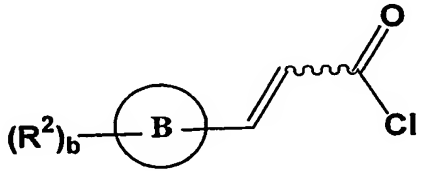
comprising:

(1) halogenating a carboxylic acid of formula VI with a halogenating agent:



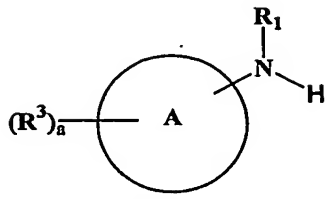
VI

to form an acid halide of formula VII:



VII

(2) coupling the acid halide VII to an aromatic amino compound of formula II

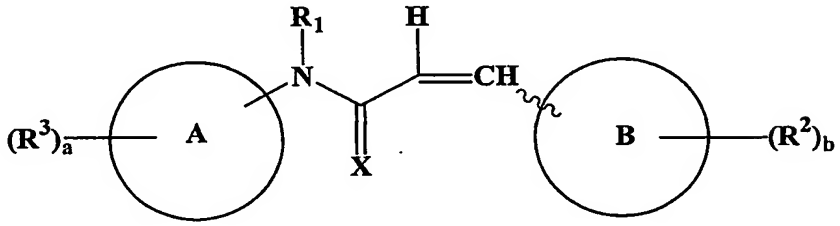


II

to form an amide compound of formula I;

or a salt of such a compound.

26. A process for preparing a compound according to claim 7, which compound has the formula I,



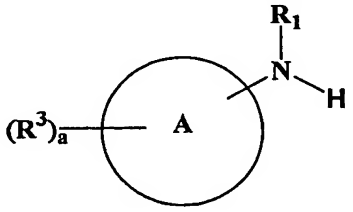
I

wherein:

R^1, R^2, R^3, a, b, X, A and B are as defined in claim 7;

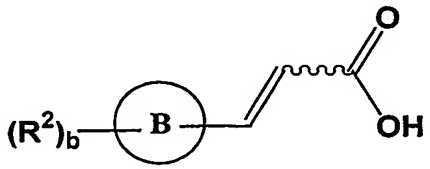
comprising:

reacting an aromatic amino compound of formula II



II

with a carboxylic acid compound of formula VI:

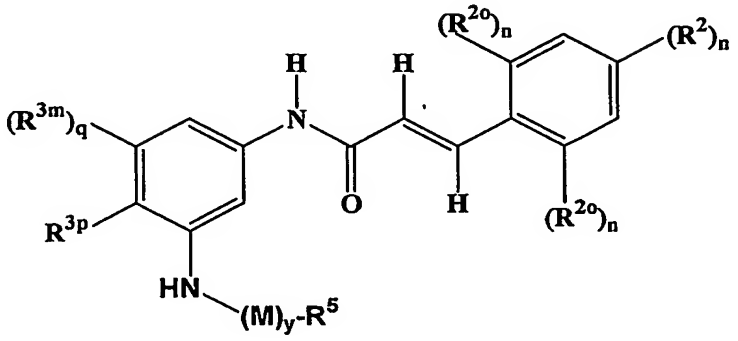


VI

and an amide coupling agent, to form a compound of formula I;

or a salt of such a compound.

27. A process for preparing a compound according to claim 21, which compound has the formula Ic:



Ic

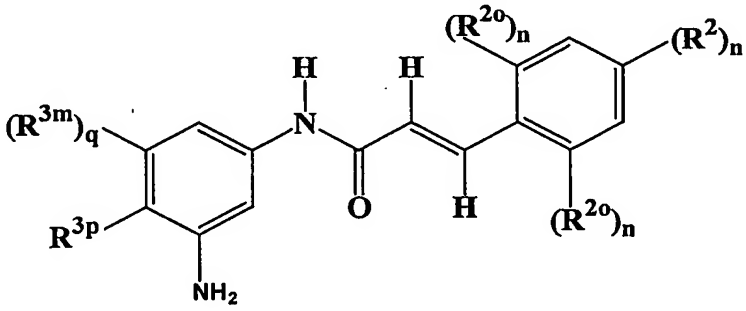
wherein:

q is 0 or 1; and

R^2, R^{2o}, R^{3m}, R^{3p}, n, M, y and R^6 are defined as in claim 21;

comprising:

reacting an aromatic amino compound of formula Id



Id

with an electrophilic compound of formula VIII:

$$R^5—L \qquad \text{VIII}$$

wherein R^5 comprises an electrophilic reactive center selected from the group consisting of:

(a) an alkyl moiety having a leaving group;

(b) an aryl or heteroaryl halide or aryl or heteroaryl pseudo halide;

(c) a carboxylic acid activated with a leaving group;

(d) a sulfonic acid activated with a leaving group;

(e) a carbamic acid moiety activated with a leaving group;

(f) a cyanate moiety;

(g) an aldehyde or ketone moiety, or a hydrate thereof or a ketal or acetal thereof;

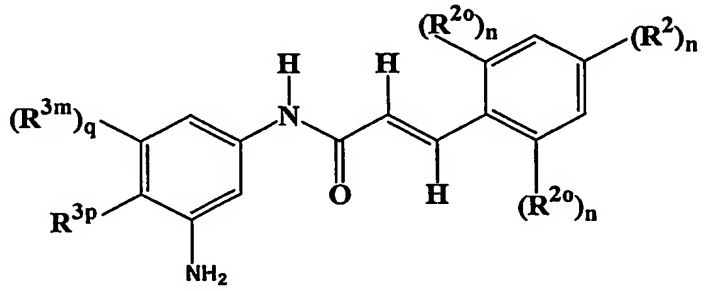
(h) a carboxylic acid moiety and an amide coupling reagent; or

(i) the intermediate product of a thiourea moiety and 2-chloro-1-methyl pyridinium iodide;

to form a compound of formula Ic,

or a salt of such a compound.

28. A process for preparing a compound according to claim 23, which compound has the formula Id:



Id

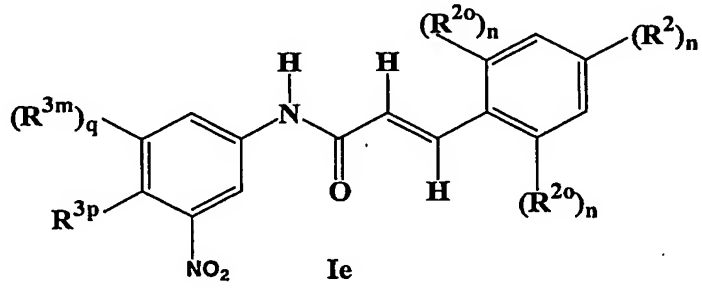
wherein:

q is 0 or 1; and

R^2, R^{2o}, R^{3m}, R^{3p} and n are defined as in claim 26;

comprising:

chemically reducing a compound of formula Ie:

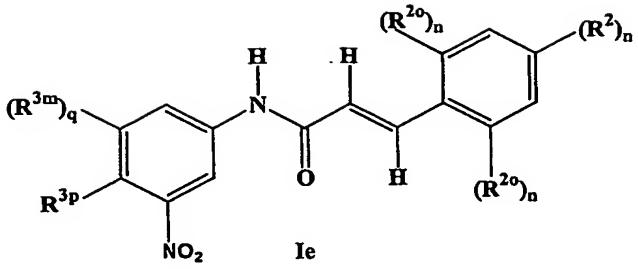


Ie

to form a compound of formula Id,

or a salt of such a compound.

29. A process for preparing a compound according to claim 16, which compound has the formula Ie:



Ie

wherein:

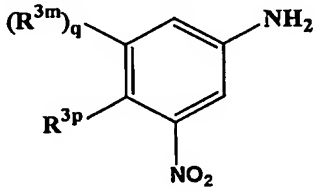
q is 0 or 1; and

R^2, R^{2o}, R^{3m}, R^{3p} and n are defined as in claim 27; and

the olefin double bond is in the *E* conformation;

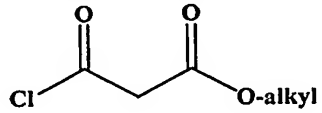
comprising:

(1) coupling a compound of formula IIb:

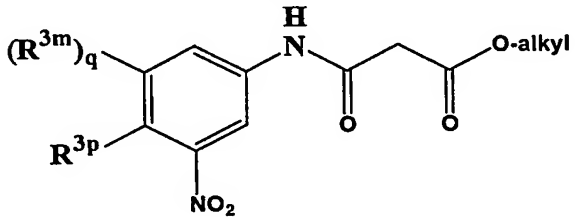


IIb

with an alkyl ester of malonic acid chloride:

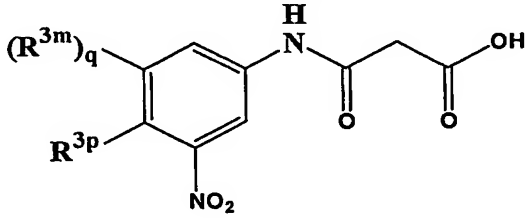


to yield a carboxylic ester compound of formula IIIb:



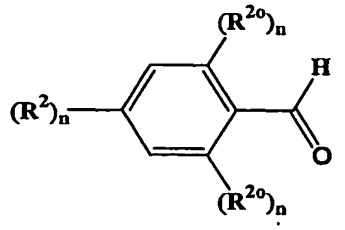
IIIb

(2) hydrolyzing the carboxylic ester compound of formula IIIb to form a carboxylic acid compound of formula IVb; and



IVb

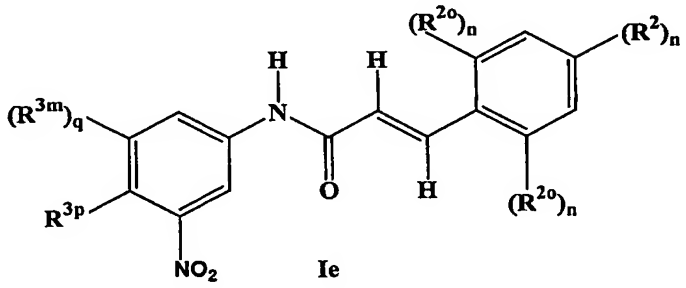
(3) coupling of the carboxylic acid compound of formula IVb with an aromatic aldehyde of formula V:



Vb

in glacial acetic acid at elevated temperature to form a compound of formula Ie; or a salt of such a compound.

30. A process for preparing a compound according to claim 16, which compound has the formula Ie:



Ie

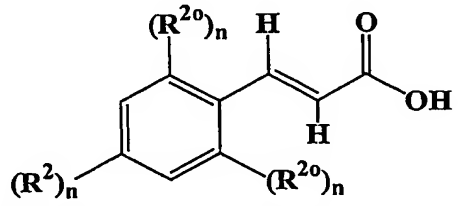
wherein:

q is 0 or 1; and

R^2, R^{2o}, R^{3m}, R^{3p} and n are defined as in claim 27;

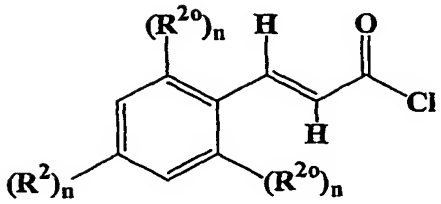
comprising:

(1) halogenating a carboxylic acid of formula VIb with a halogenating agent:



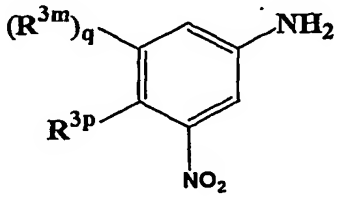
VIb

to form an acid halide of formula VIIb:



VIIb

(2) coupling the acid halide VIIb to an aromatic amino compound of formula IIb

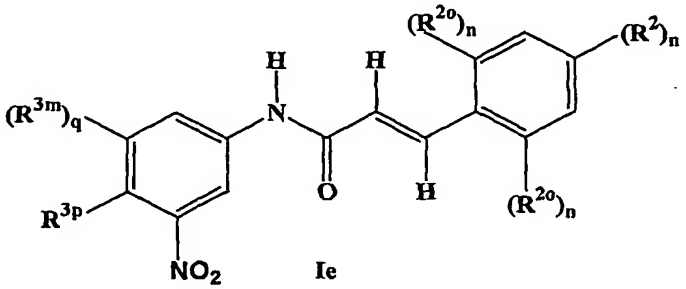


IIb

to form an amide compound of formula Ie;

or a salt of such a compound.

31. A process for preparing a compound according to claim 16, which compound has the formula Ie:



Ie

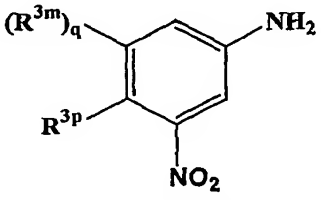
wherein:

q is 0 or 1; and

R^2, R^{2o}, R^{3m}, R^{3p} and n are defined as in claim 27;

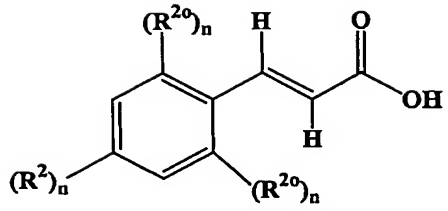
comprising:

(1) reacting an aromatic amino compound of formula IIb



IIb

with a carboxylic acid compound of formula VIb:



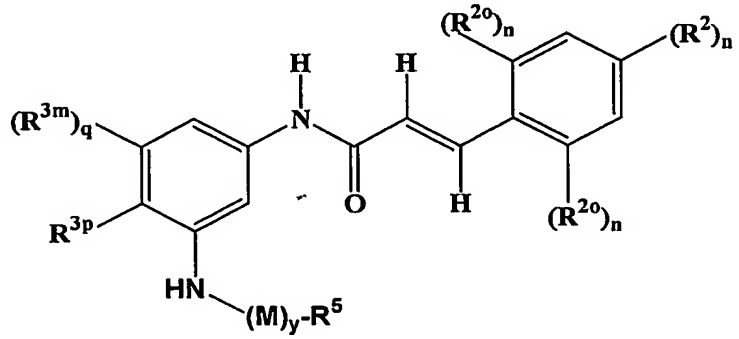
VIb

and an amide coupling agent,

to form a compound of formula Ie;

or a salt of such a compound.

32. A process for preparing a compound according to claim 21, which compound has the formula Ic:



Ic

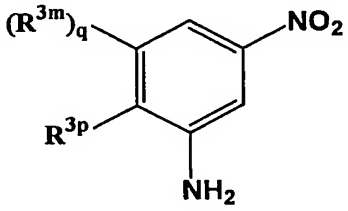
wherein:

q is 0 or 1; and

R^2, R^{2o}, R^{3m}, R^{3p}, n, M, y and R^5 are defined as in claim 21;

comprising:

(1) reacting an aromatic amine of formula IX



IX

with an electrophilic compound of formula VIII:

$$R^5—L \qquad \text{VIII}$$

wherein L comprises an electrophilic reactive center selected from the group consisting of:

(a) an alkyl moiety having a leaving group;

(b) an aryl or heteroaryl halide or aryl or heteroaryl pseudo halide;

(c) a carboxylic acid activated with a leaving group;

(d) a sulfonic acid activated with a leaving group;

(e) a carbamic acid moiety activated with a leaving group;

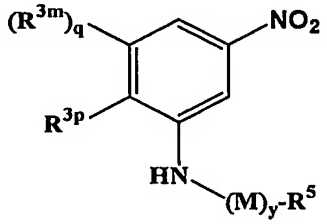
(f) a cyanate moiety;

(g) an aldehyde or ketone moiety, or a hydrate thereof or a ketal or acetal thereof;

(h) a carboxylic acid moiety and an amide coupling reagent; or

(i) the intermediate product of a thiourea moiety and 2-chloro-1-methyl pyridinium iodide;

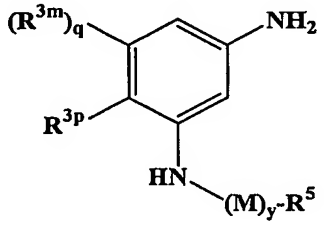
to form a compound of formula IXa:



IXa

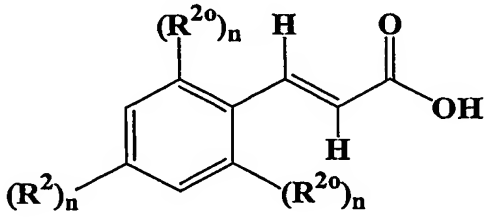
(2) optionally protecting the $-NH-(M)_y-R^5$ moiety in the formula IXa compound;

(3) chemically reducing said compound of formula IXa to form the aromatic amine IXb:



IXb

(4) reacting aromatic amine IXb with a carboxylic acid compound of formula VIb:



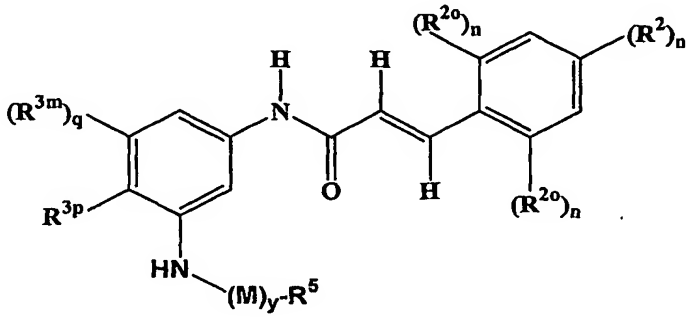
VIb

and an amide coupling agent; and

(5) optionally removing said protecting group to form a compound of formula Ic;

or a salt of such a compound.

33. A process for preparing a compound according to claim 21, which compound has the formula Ic:



Ic

wherein:

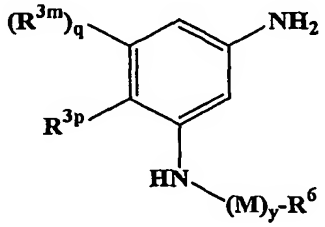
q is 0 or 1;

R^2, R^{2o}, R^{3m}, R^{3p}, n, M, y and R^5 are defined as in claim 21; and

the olefin double bond is in the *E* conformation;

comprising:

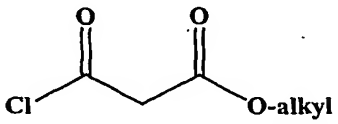
(1) coupling a compound of formula IXb:



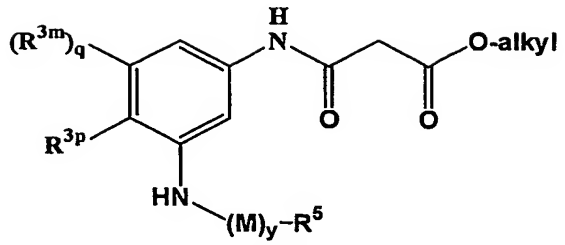
IXb

wherein the –NH-$(M)_y$-R^5 moiety is optionally protected with a protecting group;

with an alkyl ester of malonic acid chloride:

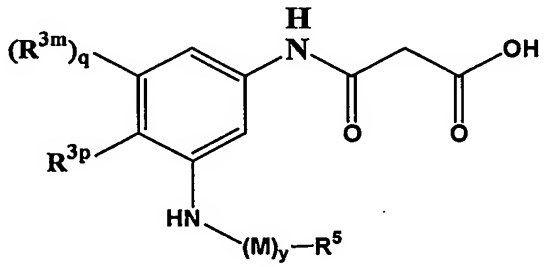


to yield a carboxylic ester compound of formula IXc:



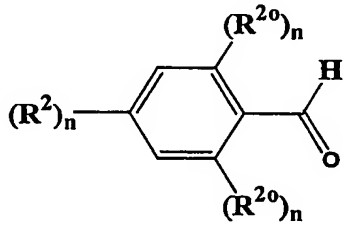
IXc

(2) hydrolyzing the carboxylic ester compound of formula IXc to form a carboxylic acid compound of formula IXd;



IXd

(3) coupling the carboxylic acid compound of formula IXd with an aromatic aldehyde of formula Vb:



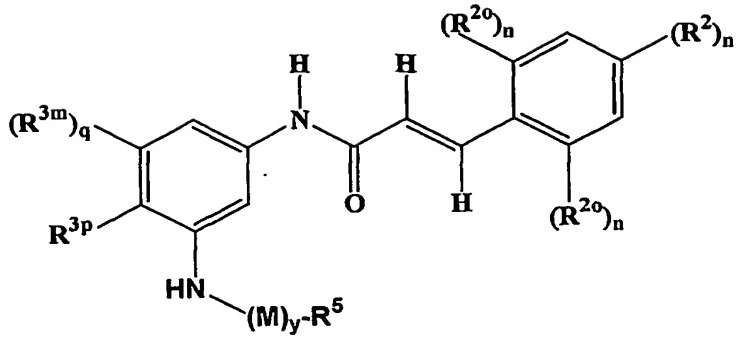
Vb

in glacial acetic acid at elevated temperature; and

(4) optionally removing said protecting group to form a compound of formula Ic;

or a salt of such a compound.

34. A process for preparing a compound according to claim 21, which compound has the formula Ic:



Ic

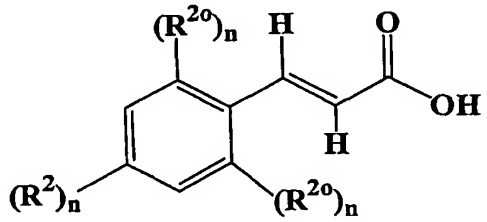
wherein:

q is 0 or 1; and

R^2, R^{2o}, R^{3m}, R^{3p}, n, M, y and R^5 are defined as in claim 21;

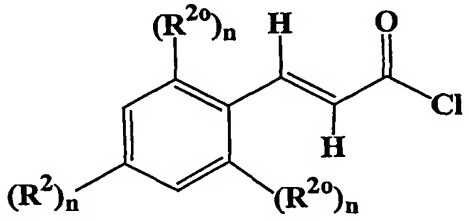
comprising:

(1) halogenating a carboxylic acid of formula VIb with a halogenating agent:



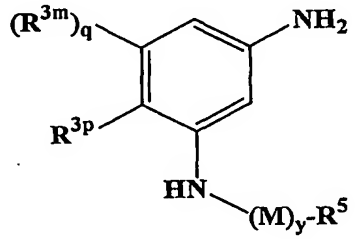
VIb

to form an acid halide of formula VIIb:



VIIb

(2) coupling the acid halide VIIb to an aromatic amino compound of formula IXb:



IXb

wherein the $-NH-(M)_y-R^5$ moiety is optionally protected with a protecting group; and

(3) optionally removing said protecting group to form an amide compound of formula Ic;

or a salt of such a compound.

35. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and at least one compound according to claim 1.

36. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and at least one compound according to claim 7.

37. A conjugate of the formula, I–L–Ab;

wherein:

I is a compound according to claim 1;

Ab is an antibody; and

–L– is a single covalent bond or a linking group covalently linking said compound to said antibody.

38. A conjugate of the formula, I–L–Ab;

wherein:

I is a compound according to claim 7;

Ab is an antibody; and

–L– is a single covalent bond or a linking group covalently linking said compound to said antibody.

39. A conjugate of the formula, Ic–L–Ab;

wherein:

Ic is a compound according to claim 21;

Ab is an antibody; and

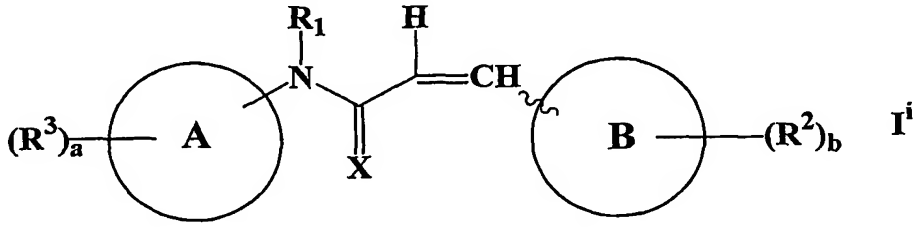
–L– is a single covalent bond or a linking group covalently linking said compound to said antibody.

40. A conjugate according to any one of claims 37, 38 or 39 wherein said antibody Ab is a monoclonal antibody or a monospecific polyclonal antibody.

41. A conjugate according to claim 40 wherein said antibody Ab is a tumor-specific antibody.

42. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and at least one conjugate according to any one of claims 37, 38 or 39.

43. A method of treating an individual for a proliferative disorder comprising administering to said individual an effective amount of at least one compound according to formula I^i,



I^i

wherein:

ring A and ring B are independently selected from the group consisting of aryl and heteroaryl;

X is O or S;

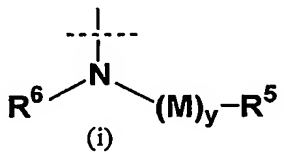
R^1 is independently selected from the group consisting of $-R^4$, $-SO_2(C_1-C_6)$alkyl, $-C(=O)R^4$, $-C(=O)OR^4$, $-C(=O)O(C_1-C_6)$alkylenearyl, $-OR^4$, $-(C_2-C_6)$alkynyl, $-(C_3-C_6)$heteroalkenyl, $-(C_2-C_6)$alkylene-OR^4, substituted aryl, unsubstituted aryl, substituted heteroaryl, unsubstituted heteroaryl, substituted aryl(C_1-C_3)alkyl, unsubstituted aryl(C_1-C_3)alkyl, substituted heteroaryl(C_1-C_3)alkyl and unsubstituted heteroaryl(C_1-C_3)alkyl;

R^2 is independently selected from -(C_1-C_6)alkyl, halogen, -OR^4, -C≡N, -NO_2, -CO_2R^4, -$C(=O)NR^4_2$, -$C(=NR^4)NR^4_2$, –O(C_1-C_3)alkylene-CO_2R^4, -(C_2-C_6)-OR^4, phosphonato, -NR^4_2, -NHC(=O)(C_1-C_6)alkyl, sulfamyl, carbamyl, -OC(=O)(C_1-C_3)alkyl, -O(C_2-C_6)-N((C_1-C_6)alkyl)$_2$, -S(C_1-C_3)alkyl, -S(=O)(C_1-C_3)alkyl and, (C_1-C_3)perfluoroalkyl -SO_2(C_1-C_3)alkyl;

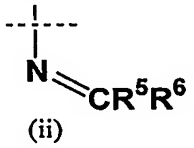
b is 1, 2, 3, 4 or 5; and

∿∿∿ indicates a single bond, whereby the compounds of formula I may be in either the E or the Z conformation;

R^3 is independently selected from halogen, -(C_1-C_6)alkyl, -OR^4 -C≡N, -$C(=NR^4)NR^4_2$, –O(C_1-C_3)alkylene-CO_2R^4, -(C_1-C_6)-OR^4, nitro, phosphonato, -NHC(=O)(C_1-C_6)alkyl, sulfamyl, -OC(=O)(C_1-C_3)alkyl, -O(C_2-C_6)-N((C_1-C_6)alkyl)$_2$, -(C_1-C_3)perfluoroalkyl and (i) or (ii) below:



(i)



(ii)

wherein:

each M is a bivalent connecting group independently selected from the group consisting of –(C_1-C_6)alkylene–, –$(CH_2)_d$-V-$(CH_2)_e$–, –$(CH_2)_f$-W-$(CH_2)_g$– and –Z–;

each y is independently selected from the group consisting of 0 and 1;

each V is independently selected from the group consisting of arylene, heteroarylene, -C(=O)-, -C(=O)(C_1-C_6)perfluoroalkylene, –C(=O)–, –C(=S)–, –S(=O)–, –SO_2–, –$C(=O)NR^4$–, –$C(=S)NR^4$– and –SO_2NR^4–;

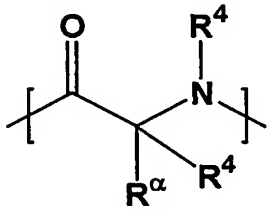
each W is independently selected from the group consisting of –NR^4–, –O– and -S–;

each d is independently selected from the group consisting of 0, 1 and 2;

each e is independently selected from the group consisting of 0, 1 and 2;

each f is independently selected from the group consisting of 1, 2 and 3;

each g is independently selected from the group consisting of 0, 1 and 2;

-Z- is  ;

wherein the absolute stereochemistry of –Z– is S or R, or a mixture of S and R;

each R^{α} is independently selected from the group consisting of -H, -(C_1-C_6)alkyl, -$(CH_2)_3$-NH-C(NH_2)(=NH), -CH_2C(=O)NH_2, -CH_2COOH, -CH_2SH, -$(CH_2)_2$C(=O)-NH_2, -$(CH_2)_2$COOH, -CH_2-(2-imidazolyl), -$(CH_2)_4$-NH_2, -$(CH_2)_2$-S-CH_3, phenyl, -CH_2-phenyl, -CH_2-OH, -CH(OH)-CH_3, -CH_2-(3-indolyl), -CH_2-(4-hydroxyphenyl); and includes compounds wherein R^{α} and R^4 combine to form a 5-, 6- or 7-membered heterocyclic or carbocyclic ring;

a is 1, 2 or 3;

R^4 is independently selected from the group consisting of –H, -(C_1-C_6)alkyl, substituted -(C_1-C_6)alkyl, -(C_2-C_6)alkenyl, substituted -(C_2-C_6)alkenyl and heteroalkyl, wherein two R^4 groups may together form a heterocycle;

each R^5 is independently selected from the group consisting of -R^4, unsubstituted aryl, substituted aryl, substituted heterocyclic, unsubstituted heterocyclic, -CO_2R^4, -C(=O)NR^4_2, -C(=NH)-NR^4_2, -(C_1-C_6)perfluoroalkyl, -CF_2Cl, -P(=O)(OR^4)$_2$, -OP(=O)(OR^4)$_2$, -$CR^4R^7R^8$ and a monovalent peptidyl moiety with a molecular weight of less than 1000; provided that when y is 0 and R^5 is –CO_2R^4; then R^4 is not –H;

each R^6 is independently selected from the group consisting of –H, -(C_1-C_6)alkyl, and aryl(C_1-C_3)alkyl;

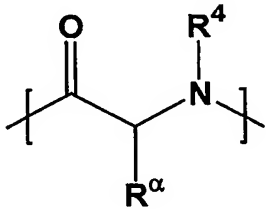
each R^7 is independently selected from the group consisting of –H, -(C_1-C_6)alkyl, –C(=O)R^8, -OR^4, -SR^4, -OC(=O)$(CH_2)_2CO_2R^6$, guanidino, -$NR^4{}_2$, -$NR^4{}_3{}^+$, -$N^+(CH_2CH_2OR^5)_3$, halogen, phenyl, substituted phenyl, heterocyclyl, and substituted heterocyclyl; and

each R^8 is independently selected from the group consisting of R^α, halogen, -$NR^4{}_2$ and heterocycles containing two nitrogen atoms;

wherein the substituents for the substituted aryl and substituted heterocyclic groups comprising or included within Ar, R^1, R^5 R^6, R^7 and R^α are independently selected from the group consisting of halogen, (C_1-C_6)alkyl, (C_1-C_6)alkoxy, -NO_2, -C≡N, -C(=O)O(C_1-C_3)alkyl, -OR^4, -(C_2-C_6)-OR^4, phosphonato, -$NR^4{}_2$, -NHC(=O)(C_1-C_6)alkyl, sulfamyl, carbamyl, -OC(=O)(C_1-C_3)alkyl, -O(C_2-C_6)-N((C_1-C_6)alkyl)$_2$ and -(C_1-C_3)perfluoroalkyl; or a salt of such a compound.

44. The method according to claim 43,

wherein:

-Z- is 

;

wherein the absolute stereochemistry of –Z– is either S or R; and

each R^α is independently selected from the group consisting of -H, -CH_3, -$(CH_2)_3$-NH-C(NH_2)(=NH), -CH_2C(=O)NH_2, -CH_2COOH, -CH_2SH, -$(CH_2)_2$C(=O)-NH_2, -$(CH_2)_2$COOH, -CH_2-(2-imidazolyl), -CH(CH_3)-CH_2CH_3, -CH_2CH(CH_3)$_2$, -$(CH_2)_4$-NH_2, -$(CH_2)_2$-S-CH_3, phenyl, CH_2-phenyl, -CH_2-OH, -CH(OH)-CH_3, -CH_2-(3-indolyl), -CH_2-(4-hydroxyphenyl), -CH(CH_3)$_2$ and –CH_2CH_3; and includes compounds wherein R^α and R^4 combine to form a 5-, 6- or 7-membered heterocyclic ring;

b is 1, 2 or 3;

each R^7 is independently selected from the group consisting of –H, -(C_1-C_6)alkyl and -(C_1-C_6)acyl;

each V is independently selected from the group consisting of –C(=O)–, –C(=S)–, –S(=O)–, –SO_2–, –C(=O)NR^4–, –C(=S)NR^4– and –SO_2NR^4–;

each R^5 is independently selected from the group consisting of -R^4, unsubstituted aryl, substituted aryl, substituted heterocyclic, unsubstituted heterocyclic, -CO_2R^4, -C(=O)NR^4_2, -C(=NH)-NR^4_2, and a monovalent peptidyl moiety with a molecular weight of less than 1000; provided that when y is 0 and R^5 is –CO_2R^4; then R^4 is not –H; and

wherein the substituents for the substituted aryl and substituted heterocyclic groups comprising or included within Ar, R^1, R^5 and R^α are independently selected from the group consisting of halogen, -(C_1-C_6)alkyl, -(C_1-C_6)alkoxy, -NO_2, -C≡N, -C(=O)O(C_1-C_3)alkyl, -OR^4, -(C_2-C_6)-OR^4, phosphonato, -NR^4_2, -NHC(=O)(C_1-C_6)alkyl, sulfamyl, carbamyl, -OC(=O)(C_1-C_3)alkyl, -O(C_2-C_6)-N((C_1-C_6)alkyl)$_2$ and -(C_1-C_3)perfluoroalkyl; or a salt of such a compound.

45. A method according to claim 43 wherein the proliferative disorder is selected from the group consisting of hemangiomatosis in newborn; secondary progressive multiple sclerosis; chronic progressive myelodegenerative disease; neurofibromatosis; ganglioneuromatosis; keloid formation; Paget's Disease of the bone; fibrocystic disease, sarcoidosis; Peronies and Duputren's fibrosis, cirrhosis, atherosclerosis and vascular restenosis.

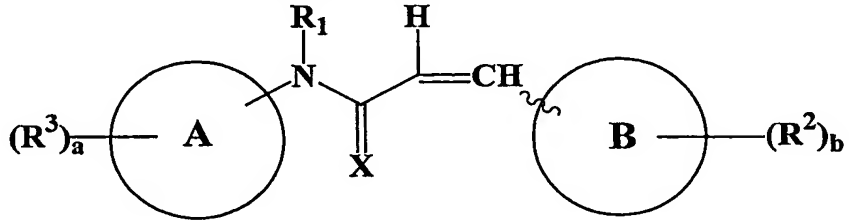
46. A method according to claim 45 wherein the proliferative disorder is cancer.

47. A method of according to claim 46 wherein the cancer is selected from the group of ovarian cancer, breast cancer, prostate cancer, lung cancer, renal cancer, colorectal cancer, brain cancer and leukemia.

48. The method of claim 43, further comprising administering an effective amount of therapeutic ionizing radiation to the individual.

49. The method of claim 48 wherein the proliferative disorder is cancer.

50. A method of selectively inducing apoptosis of tumor cells in an individual afflicted with cancer comprising administering to said individual an effective amount of at least one compound of formula I^{ii}



I^{ii}

wherein:

ring A and ring B are independently selected from the group consisting of aryl and heteroaryl;

X is O or S;

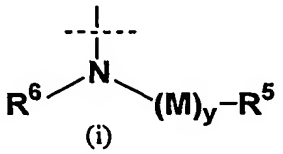
R^1 is independently selected from the group consisting of $-R^4$, $-SO_2(C_1-C_6)$alkyl, $-C(=O)R^4$, $-C(=O)OR^4$, $-C(=O)O(C_1-C_6)$alkylenearyl, $-OR^4$, $-(C_2-C_6)$alkynyl, $-(C_3-C_6)$heteroalkenyl, $-(C_2-C_6)$alkylene-OR^4, substituted aryl, unsubstituted aryl, substituted heteroaryl, unsubstituted heteroaryl, substituted aryl(C_1-C_3)alkyl, unsubstituted aryl(C_1-C_3)alkyl, substituted heteroaryl(C_1-C_3)alkyl and unsubstituted heteroaryl(C_1-C_3)alkyl;

R^2 is independently selected from $-(C_1-C_6)$alkyl, halogen, $-OR^4$, $-C\equiv N$, $-NO_2$, $-CO_2R^4$, $-C(=O)NR^4{}_2$, $-C(=NR^4)NR^4{}_2$, $-O(C_1-C_3)$alkylene-CO_2R^4, $-(C_2-C_6)-OR^4$, phosphonato, $-NR^4{}_2$, $-NHC(=O)(C_1-C_6)$alkyl, sulfamyl, carbamyl, $-OC(=O)(C_1-C_3)$alkyl, $-O(C_2-C_6)-N((C_1-C_6)\text{alkyl})_2$, $-S(C_1-C_3)$alkyl, $-S(=O)(C_1-C_3)$alkyl, $-(C_1-C_3)$perfluoroalkyl and $-SO_2(C_1-C_3)$alkyl;

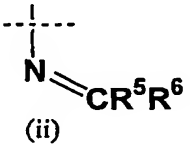
b is 1, 2, 3, 4 or 5; and

∿∿∿ indicates a single bond, whereby the compounds of formula I may be in either the E or the Z conformation;

R^3 is independently selected from halogen, -(C_1-C_6)alkyl, -OR^4 -C≡N, -C(=O)NR^4_2, -C(=O)OR^4, -C(=NR^4)NR^4_2, –O(C_1-C_3)alkylene-CO_2R^4, -(C_1-C_6)-OR^4, nitro, phosphonato, -NHC(=O)(C_1-C_6)alkyl, sulfamyl, -OC(=O)(C_1-C_3)alkyl, -O(C_2-C_6)-N((C_1-C_6)alkyl)$_2$, -(C_1-C_3)perfluoroalkyl and (i) or (ii) below:



(i)



(ii)

wherein:

each M is a bivalent connecting group independently selected from the group consisting of –(C_1-C_6)alkylene–, –$(CH_2)_d$-V-$(CH_2)_e$–, –$(CH_2)_f$-W-$(CH_2)_g$– and –Z–;

each y is independently selected from the group consisting of 0 and 1;

each V is independently selected from the group consisting of arylene, heteroarylene, -C(=O)-, -C(=O)(C_1-C_6)perfluoroalkylene, –C(=O)–, –C(=S)–, –S(=O)–, –SO_2–, –C(=O)NR^4–, –C(=S)NR^4– and –SO_2NR^4–;

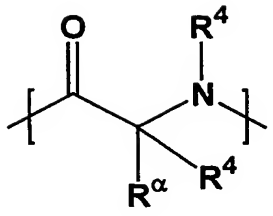
each W is independently selected from the group consisting of –NR^4–, –O– and -S–;

each d is independently selected from the group consisting of 0, 1 and 2;

each e is independently selected from the group consisting of 0, 1 and 2;

each f is independently selected from the group consisting of 1, 2 and 3;

each g is independently selected from the group consisting of 0, 1 and 2;

-Z- is  ;

wherein the absolute stereochemistry of –Z– is S or R, or a mixture of S and R;

each R^{α} is independently selected from the group consisting of -H, -(C_1-C_6)alkyl, -$(CH_2)_3$-NH-$C(NH_2)$(=NH), -CH_2C(=O)NH_2, -CH_2COOH, -CH_2SH, -$(CH_2)_2C$(=O)-NH_2, -$(CH_2)_2COOH$, -CH_2-(2-imidazolyl), -$(CH_2)_4$-NH_2, -$(CH_2)_2$-S-CH_3, phenyl, -CH_2-phenyl, -CH_2-OH, -CH(OH)-CH_3, -CH_2-(3-indolyl), -CH_2-(4-hydroxyphenyl); and includes compounds wherein R^{α} and R^4 combine to form a 5-, 6- or 7-membered heterocyclic or carbocyclic ring;

a is 1, 2 or 3;

R^4 is independently selected from the group consisting of –H, -(C_1-C_6)alkyl, substituted -(C_1-C_6)alkyl, -(C_2-C_6)alkenyl, substituted -(C_2-C_6)alkenyl and heteroalkyl, wherein two R^4 groups may together form a heterocycle;

each R^5 is independently selected from the group consisting of -R^4, unsubstituted aryl, substituted aryl, substituted heterocyclic, unsubstituted heterocyclic, -CO_2R^4, -C(=O)NR^4_2, -C(=NH)-NR^4_2, -(C_1-C_6)perfluoroalkyl, -CF_2Cl, -P(=O)$(OR^4)_2$, -OP(=O)$(OR^4)_2$, -$CR^4R^7R^8$ and a monovalent peptidyl moiety with a molecular weight of less than 1000; provided that when y is 0 and R^5 is –CO_2R^4; then R^4 is not –H;

each R^6 is independently selected from the group consisting of –H, -(C_1-C_6)alkyl, and aryl(C_1-C_3)alkyl;

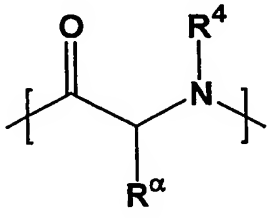
each R^7 is independently selected from the group consisting of –H, -(C_1-C_6)alkyl, –C(=O)R^8, -OR^4, -SR^4, -OC(=O)$(CH_2)_2CO_2R^6$, guanidino, -NR^4_2, -$NR^4_3{}^+$, -$N^+(CH_2CH_2OR^5)_3$, halogen, phenyl, substituted phenyl, heterocyclyl, and substituted heterocyclyl; and

each R^8 is independently selected from the group consisting of R^{α}, halogen, -NR^4_2 and heterocycles containing two nitrogen atoms;

wherein the substituents for the substituted aryl and substituted heterocyclic groups comprising or included within Ar, R^1, R^5 R^6, R^7 and R^α are independently selected from the group consisting of halogen, -(C_1-C_6)alkyl, -(C_1-C_6)alkoxy, -NO_2, -C≡N, -C(=O)O(C_1-C_3)alkyl, -OR^4, -(C_2-C_6)-OR^4, phosphonato, -NR^4_2, -NHC(=O)(C_1-C_6)alkyl, sulfamyl, carbamyl, -OC(=O)(C_1-C_3)alkyl, -O(C_2-C_6)-N((C_1-C_6)alkyl)$_2$ and -(C_1-C_3)perfluoroalkyl; or a salt of such a compound.

51. The method according to claim 50,

wherein –Z– is:



;

wherein the absolute stereochemistry of –Z– is either S or R; and

each R^α is independently selected from the group consisting of -H, -CH_3, -(CH_2)$_3$-NH-C(NH_2)(=NH), -CH_2C(=O)NH_2, -CH_2COOH, -CH_2SH, -(CH_2)$_2$C(=O)-NH_2, -(CH_2)$_2$COOH, -CH_2-(2-imidazolyl), -CH(CH_3)-CH_2CH_3, -CH_2CH(CH_3)$_2$, -(CH_2)$_4$-NH_2, -(CH_2)$_2$-S-CH_3, phenyl, -CH_2-phenyl, -CH_2-OH, -CH(OH)-CH_3, -CH_2-(3-indolyl), -CH_2-(4-hydroxyphenyl), -CH(CH_3)$_2$ and –CH_2CH_3; and includes compounds wherein R^α and R^4 combine to form a 5-, 6- or 7-membered heterocyclic ring;

b is 1, 2 or 3;

each R^7 is independently selected from the group consisting of –H, -(C_1-C_6)alkyl and -(C_1-C_6)acyl;

each V is independently selected from the group consisting of –C(=O)–, –C(=S)–, –S(=O)–, –SO_2–, –C(=O)NR^4–, –C(=S)NR^4– and –SO_2NR^4–;

each R^5 is independently selected from the group consisting of -R^4, unsubstituted aryl, substituted aryl, substituted heterocyclic, unsubstituted heterocyclic, -CO_2R^4, -C(=O)NR^4_2, -C(=NH)-NR^4_2, and a monovalent peptidyl

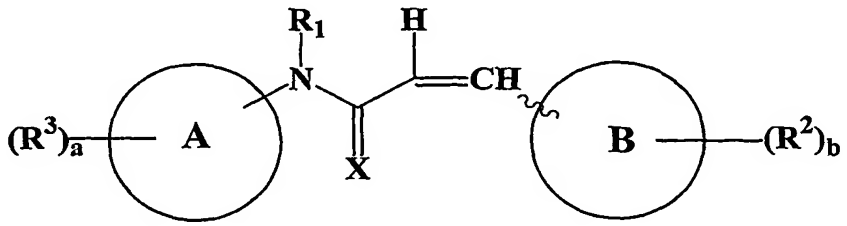
moiety with a molecular weight of less than 1000; provided that when y is 0 and R^5 is $-CO_2R^4$; then R^4 is not –H; and

wherein the substituents for the substituted aryl and substituted heterocyclic groups comprising or included within Ar, R^1, R^5 and R^α are independently selected from the group consisting of halogen, -(C_1-C_6)alkyl, -(C_1-C_6)alkoxy, $-NO_2$, -C≡N, -C(=O)O(C_1-C_3)alkyl, $-OR^4$, -(C_2-C_6)-OR^4, phosphonato, $-NR^4_2$, -NHC(=O)(C_1-C_6)alkyl, sulfamyl, carbamyl, -OC(=O)(C_1-C_3)alkyl, -O(C_2-C_6)-N((C_1-C_6)alkyl)$_2$ and -(C_1-C_3)perfluoroalkyl; or a salt of such a compound.

52. A method according to claim 50 wherein the tumor cells are selected from the group of tumors consisting of tumors of the ovarian, breast, prostate, lung, colorectal, renal and brain tumors

53. A method of treating an individual afflicted with cancer, comprising administering to said individual an effective amount of at least one conjugate according to any one of claims 37, 38 or 39.

54. A method of reducing or eliminating the effects of ionizing radiation on normal cells in a subject who has incurred or is at risk of incurring exposure to ionizing radiation, comprising administering to the subject an effective amount of at least one radioprotective compound according to formula I^{ii} to the subject prior to or after exposure to ionizing radiation:



I^{ii}

wherein:

ring A and ring B are independently selected from the group consisting of aryl and heteroaryl;

X is O or S;

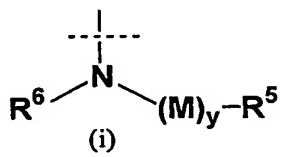
R^1 is independently selected from the group consisting of $-R^4$, $-SO_2(C_1-C_6)$alkyl, $C(=O)R^4$, $-C(=O)OR^4$, $-C(=O)O(C_1-C_6)$alkylenearyl, $-OR^4$, $-(C_2-C_6)$alkynyl, $-(C_3-C_6)$heteroalkenyl, $-(C_2-C_6)$alkylene-OR^4, substituted aryl, unsubstituted aryl, substituted heteroaryl, unsubstituted heteroaryl, substituted aryl(C_1-C_3)alkyl, unsubstituted aryl(C_1-C_3)alkyl, substituted heteroaryl(C_1-C_3)alkyl and unsubstituted heteroaryl(C_1-C_3)alkyl;

R^2 is independently selected from $-(C_1-C_6)$alkyl, halogen, $-OR^4$, $-C\equiv N$, $-NO_2$, $-CO_2R^4$, $-C(=O)NR^4{}_2$, $-C(=NR^4)NR^4{}_2$, $-O(C_1-C_3)$alkylene-CO_2R^4, $-(C_2-C_6)$-OR^4, phosphonato, $-NR^4{}_2$, $-NHC(=O)(C_1-C_6)$alkyl, sulfamyl, carbamyl, $-OC(=O)(C_1-C_3)$alkyl, $-O(C_2-C_6)$-$N((C_1-C_6)\text{alkyl})_2$, $-S(C_1-C_3)$alkyl, $-S(=O)(C_1-C_3)$alkyl (C_1-C_3)perfluoroalkyl and $-SO_2(C_1-C_3)$alkyl;

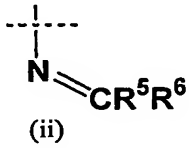
b is 1, 2, 3, 4 or 5; and

∿∿∿ indicates a single bond, whereby the compounds of formula I may be in either the E or the Z conformation;

R^3 is independently selected from halogen, $-(C_1-C_6)$alkyl, $-OR^4$ $-C\equiv N$, $-C(=O)NR^4{}_2$, $-C(=O)OR^4$, $-C(=NR^4)NR^4{}_2$, $-O(C_1-C_3)$alkylene-CO_2R^4, $-(C_1-C_6)$-OR^4, nitro, phosphonato, $-NHC(=O)(C_1-C_6)$alkyl, sulfamyl, carbamyl, $-OC(=O)(C_1-C_3)$alkyl, $-O(C_2-C_6)$-$N((C_1-C_6)\text{alkyl})_2$, $-(C_1-C_3)$perfluoroalkyl and (i) or (ii) below:



(i)



(ii)

wherein:

each M is a bivalent connecting group independently selected from the group consisting of $-(C_1-C_6)$alkylene–, $-(CH_2)_d$-V-$(CH_2)_e-$; $-(CH_2)_f$-W-$(CH_2)_g-$ and –Z–;

each y is independently selected from the group consisting of 0 and 1;

each V is independently selected from the group consisting of arylene, heteroarylene, -C(=O)-, $-C(=O)(C_1-C_6)$perfluoroalkylene,

–C(=O)–, –C(=S)–, –S(=O)–, $–SO_2–$, –C(=O)NR^4–, –C(=S)NR^4– and $–SO_2NR^4–$;

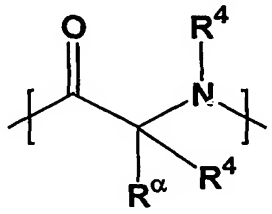
each W is independently selected from the group consisting of $–NR^4–$, –O– and -S–;

each d is independently selected from the group consisting of 0, 1 and 2;

each e is independently selected from the group consisting of 0, 1 and 2;

each f is independently selected from the group consisting of 1, 2 and 3;

each g is independently selected from the group consisting of 0, 1 and 2;

-Z- is 

;

wherein the absolute stereochemistry of –Z– is S or R, or a mixture of S and R;

each R^α is independently selected from the group consisting of -H, -(C_1-C_6)alkyl, $-(CH_2)_3$-NH-C(NH_2)(=NH), $-CH_2C(=O)NH_2$, $-CH_2COOH$, $-CH_2SH$, $-(CH_2)_2C(=O)-NH_2$, $-(CH_2)_2COOH$, $-CH_2$-(2-imidazolyl), $-(CH_2)_4-NH_2$, $-(CH_2)_2$-S-CH_3, phenyl, CH_2-phenyl, $-CH_2-OH$, -CH(OH)-CH_3, $-CH_2$-(3-indolyl), $-CH_2$-(4-hydroxyphenyl); and includes compounds wherein R^α and R^4 combine to form a 5-, 6- or 7-membered heterocyclic or carbocyclic ring;

a is 1, 2 or 3;

R^4 is independently selected from the group consisting of –H, -(C_1-C_6)alkyl, substituted -(C_1-C_6)alkyl, -(C_2-C_6)alkenyl, substituted -(C_2-C_6)alkenyl and heteroalkyl, wherein two R^4 groups may together form a heterocycle;

each R^5 is independently selected from the group consisting of -R^4, unsubstituted aryl, substituted aryl, substituted heterocyclic, unsubstituted

heterocyclic, $-CO_2R^4$, $-C(=O)NR^4{}_2$, $-C(=NH)-NR^4{}_2$, $-(C_1-C_6)$perfluoroalkyl, $-CF_2Cl$, $-P(=O)(OR^4)_2$, $-OP(=O)(OR^4)_2$, $-CR^4R^7R^8$ and a monovalent peptidyl moiety with a molecular weight of less than 1000; provided that when y is 0 and R^5 is $-CO_2R^4$; then R^4 is not –H;

each R^6 is independently selected from the group consisting of –H, $-(C_1-C_6)$alkyl, and aryl(C_1-C_3)alkyl;

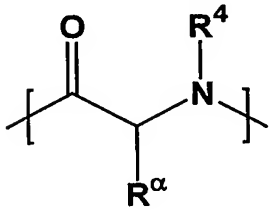
each R^7 is independently selected from the group consisting of –H, $-(C_1-C_6)$alkyl, $-C(=O)R^8$, $-OR^4$, $-SR^4$, $-OC(=O)(CH_2)_2CO_2R^6$, guanidino, $-NR^4{}_2$, $-NR^4{}_3{}^+$, $-N^+(CH_2CH_2OR^5)_3$, halogen, phenyl, substituted phenyl, heterocyclyl, and substituted heterocyclyl; and

each R^8 is independently selected from the group consisting of R^α, halogen, $-NR^4{}_2$ and heterocycles containing two nitrogen atoms;

wherein the substituents for the substituted aryl and substituted heterocyclic groups comprising or included within Ar, R^1, R^5 R^6, R^7 and R^α are independently selected from the group consisting of halogen, $-(C_1-C_6)$alkyl, $-(C_1-C_6)$alkoxy, $-NO_2$, $-C\equiv N$, $-C(=O)O(C_1-C_3)$alkyl, $-OR^4$, $-(C_2-C_6)-OR^4$, phosphonato, $-NR^4{}_2$, $-NHC(=O)(C_1-C_6)$alkyl, sulfamyl, carbamyl, $-OC(=O)(C_1-C_3)$alkyl, $-O(C_2-C_6)-N((C_1-C_6)\text{alkyl})_2$ and $-(C_1-C_3)$perfluoroalkyl; or a salt of such a compound.

55. The method according to claim 54,

wherein –Z– is:



;

wherein the absolute stereochemistry of –Z– is either S or R; and

each R^α is independently selected from the group consisting of -H, $-CH_3$, $-(CH_2)_3-NH-C(NH_2)(=NH)$, $-CH_2C(=O)NH_2$, $-CH_2COOH$, $-CH_2SH$, $-(CH_2)_2C(=O)-NH_2$, $-(CH_2)_2COOH$, $-CH_2$-(2-imidazolyl), $-CH(CH_3)-CH_2CH_3$,

$-CH_2CH(CH_3)_2$, $-(CH_2)_4-NH_2$, $-(CH_2)_2-S-CH_3$, phenyl, $-CH_2$-phenyl, $-CH_2-OH$, $-CH(OH)-CH_3$, $-CH_2$-(3-indolyl), $-CH_2$-(4-hydroxyphenyl), $-CH(CH_3)_2$ and $-CH_2CH_3$; and includes compounds wherein R^α and R^4 combine to form a 5-, 6- or 7-membered heterocyclic ring;

b is 1, 2 or 3;

each R^7 is independently selected from the group consisting of –H, $-(C_1-C_6)$alkyl and $-(C_1-C_6)$acyl;

each V is independently selected from the group consisting of $-C(=O)-$, $-C(=S)-$, $-S(=O)-$, $-SO_2-$, $-C(=O)NR^4-$, $-C(=S)NR^4-$ and $-SO_2NR^4-$;

each R^5 is independently selected from the group consisting of $-R^4$, unsubstituted aryl, substituted aryl, substituted heterocyclic, unsubstituted heterocyclic, $-CO_2R^4$, $-C(=O)NR^4_2$, $-C(=NH)-NR^4_2$, and a monovalent peptidyl moiety with a molecular weight of less than 1000; provided that when y is 0 and R^5 is $-CO_2R^4$; then R^4 is not –H; and

wherein the substituents for the substituted aryl and substituted heterocyclic groups comprising or included within Ar, R^1, R^5 and R^α are independently selected from the group consisting of halogen, $-(C_1-C_6)$alkyl, (C_1-C_6)alkoxy, $-NO_2$, $-C\equiv N$, $-C(=O)O(C_1-C_3)$alkyl, $-OR^4$, $-(C_2-C_6)-OR^4$, phosphonato, $-NR^4_2$, $-NHC(=O)(C_1-C_6)$alkyl, sulfamyl, carbamyl, $-OC(=O)(C_1-C_3)$alkyl, $-O(C_2-C_6)-N((C_1-C_6)\text{alkyl})_2$ and $-(C_1-C_3)$perfluoroalkyl; or a salt of such a compound.

56. The method of claim 54 wherein the radioprotective compound is administered before the subject is exposed to the ionizing radiation.

57. The method of claim 56, wherein the radioprotective compound is administered at least about six hours before the subject is exposed to the ionizing radiation.

58. The method of claim 57, wherein the radioprotective compound is administered no more than about twenty-four hours before the subject is exposed to the ionizing radiation.

59. The method of claim 58, wherein the radioprotective compound is administered about eighteen and about six hours before the subject is exposed to the ionizing radiation.

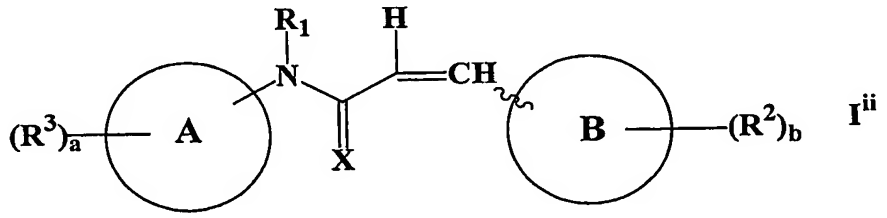
60. The method of claim 54 wherein the radioprotective compound is administered after the subject is exposed to the ionizing radiation.

61. The method of claim 60, wherein the radioprotective compound is administered between zero and six hours after the subject is exposed to the ionizing radiation.

62. A method of reducing the number of malignant cells in bone marrow of a subject, comprising:

(1) removing a portion of the subject's bone marrow;

(2) administering an effective amount of at least one radioprotective aryl or heteroaryl propene amide of formula I^{ii}



I^{ii}

wherein:

ring A and ring B are independently selected from the group consisting of aryl and heteroaryl;

X is O or S;

R^1 is independently selected from the group consisting of $-R^4$, $-SO_2(C_1-C_6)$alkyl, $-C(=O)R^4$, $-C(=O)OR^4$, $-C(=O)O(C_1-C_6)$alkylenearyl, $-OR^4$, $-(C_2-C_6)$alkynyl, $-(C_3-C_6)$heteroalkenyl, $-(C_2-C_6)$alkylene-OR^4, substituted aryl,

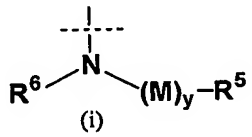
unsubstituted aryl, substituted heteroaryl, unsubstituted heteroaryl, substituted aryl(C_1-C_3)alkyl, unsubstituted aryl(C_1-C_3)alkyl, substituted heteroaryl(C_1-C_3)alkyl and unsubstituted heteroaryl(C_1-C_3)alkyl;

R^2 is independently selected from -(C_1-C_6)alkyl, halogen, -OR^4, -C≡N, -NO_2, -CO_2R^4, -C(=O)NR^4_2, -C(=NR^4)NR^4_2, –O(C_1-C_3)alkylene-CO_2R^4, -(C_2-C_6)-OR^4, phosphonato, -NR^4_2, -NHC(=O)(C_1-C_6)alkyl, sulfamyl, carbamyl, -OC(=O)(C_1-C_3)alkyl, -O(C_2-C_6)-N((C_1-C_6)alkyl)$_2$, -S(C_1-C_3)alkyl, -S(=O)(C_1-C_3)alkyl -(C_1-C_3)perfluoroalkyl and -SO_2(C_1-C_3)alkyl;

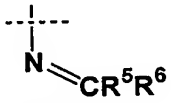
b is 1, 2, 3, 4 or 5;

∿∿∿ indicates a single bond, whereby the compounds of formula I may be in either the E or the Z conformation;

R^3 is independently selected from halogen, -(C_1-C_6)alkyl, -OR^4 -C≡N, -C(=O)NR^4_2, -C(=O)OR^4, -C(=NR^4)NR^4_2, –O(C_1-C_3)alkylene-CO_2R^4, -(C_1-C_6)-OR^4, nitro, phosphonato, -NHC(=O)(C_1-C_6)alkyl, sulfamyl, carbamyl, -OC(=O)(C_1-C_3)alkyl, -O(C_2-C_6)-N((C_1-C_6)alkyl)$_2$, -(C_1-C_3)perfluoroalkyl and (i) or (ii) below:



(i)



(ii)

wherein:

each M is a bivalent connecting group independently selected from the group consisting of –(C_1-C_6)alkylene–, –(CH_2)$_d$-V-(CH_2)$_e$–, –(CH_2)$_f$-W-(CH_2)$_g$– and –Z–;

each y is independently selected from the group consisting of 0 and 1;

each V is independently selected from the group consisting of arylene, heteroarylene, -C(=O)-, -C(=O)(C_1-C_6)perfluoroalkylene, –C(=O)–, –C(=S)–, –S(=O)–, –SO_2–, –C(=O)NR^4–, –C(=S)NR^4– and –SO_2NR^4–;

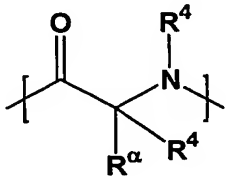
each W is independently selected from the group consisting of –NR^4–, –O– and -S–;

each d is independently selected from the group consisting of 0, 1 and 2;

each e is independently selected from the group consisting of 0, 1 and 2;

each f is independently selected from the group consisting of 1, 2 and 3;

each g is independently selected from the group consisting of 0, 1 and 2;

-Z- is  ;

wherein the absolute stereochemistry of –Z– is S or R, or a mixture of S and R;

each R^{α} is independently selected from the group consisting of -H, -(C_1-C_6)alkyl, -$(CH_2)_3$-NH-$C(NH_2)$(=NH), -CH_2C(=O)NH_2, -CH_2COOH, -CH_2SH, -$(CH_2)_2C$(=O)-NH_2, -$(CH_2)_2COOH$, -CH_2-(2-imidazolyl), -$(CH_2)_4$-NH_2, -$(CH_2)_2$-S-CH_3, phenyl, CH_2-phenyl, -CH_2-OH, -CH(OH)-CH_3, -CH_2-(3-indolyl), -CH_2-(4-hydroxyphenyl); and includes compounds wherein R^{α} and R^4 combine to form a 5-, 6- or 7-membered heterocyclic or carbocyclic ring;

a is 1, 2 or 3;

R^4 is independently selected from the group consisting of –H, -(C_1-C_6)alkyl, substituted -(C_1-C_6)alkyl, -(C_2-C_6)alkenyl, substituted -(C_2-C_6)alkenyl and heteroalkyl, wherein two R^4 groups may together form a heterocycle;

each R^5 is independently selected from the group consisting of -R^4, unsubstituted aryl, substituted aryl, substituted heterocyclic, unsubstituted heterocyclic, -CO_2R^4, -C(=O)$NR^4{}_2$, -C(=NH)-$NR^4{}_2$, -(C_1-C_6)perfluoroalkyl, -CF_2Cl, -P(=O)$(OR^4)_2$, -OP(=O)$(OR^4)_2$, -$CR^4R^7R^8$ and a monovalent peptidyl moiety with a molecular weight of less than 1000; provided that when y is 0 and R^5 is –CO_2R^4; then R^4 is not –H;

each R^6 is independently selected from the group consisting of –H, -(C_1-C_6)alkyl, and aryl(C_1-C_3)alkyl;

each R^7 is independently selected from the group consisting of –H, -(C_1-C_6)alkyl, –C(=O)R^8, -OR^4, -SR^4, -OC(=O)$(CH_2)_2CO_2R^6$, guanidino, -NR^4_2, -$NR^4_3{}^+$, -$N^+(CH_2CH_2OR^5)_3$, halogen, phenyl, substituted phenyl, heterocyclyl, and substituted heterocyclyl; and

each R^8 is independently selected from the group consisting of R^α, halogen, -NR^4_2 and heterocycles containing two nitrogen atoms;

wherein the substituents for the substituted aryl and substituted heterocyclic groups comprising or included within Ar, R^1, R^5 R^6, R^7 and R^α are independently selected from the group consisting of halogen, -(C_1-C_6)alkyl, -(C_1-C_6)alkoxy, -NO_2, -C≡N, -C(=O)O(C_1-C_3)alkyl, -OR^4, -(C_2-C_6)-OR^4, phosphonato, -NR^4_2, -NHC(=O)(C_1-C_6)alkyl, sulfamyl, carbamyl, -OC(=O)(C_1-C_3)alkyl, -O(C_2-C_6)-N((C_1-C_6)alkyl)$_2$ and -(C_1-C_3)perfluoroalkyl; or a salt of such a compound; and

to the bone marrow; and

(3) irradiating the bone marrow with an effective amount of ionizing radiation.

63. The method of claim 62, further comprising reimplanting the bone marrow into the subject.

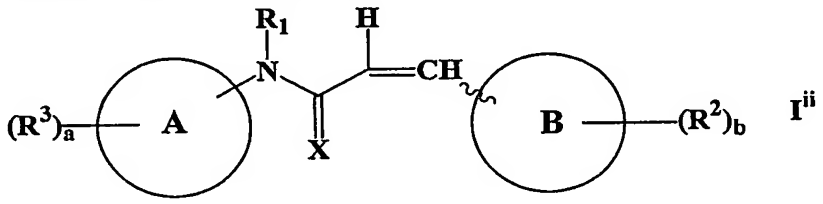
64. The method of claim 62, wherein the subject receives therapeutic ionizing radiation prior to reimplantation of the bone marrow, and is administered at least one radioprotective aryl or heteroaryl propene amide of formula I^{ii} prior to receiving the therapeutic ionizing radiation.

65. The method of claim 62 wherein the radioprotective compound is administered at least about 6 hours before exposure of the bone marrow to the ionizing radiation.

66. The method of to claim 62 wherein the radioprotective compound is administered about 20 hours before exposure to the ionizing radiation.

67. The method of claim 62 wherein the radioprotective compound is administered about 24 hours before exposure to the ionizing radiation.

68. A method for protecting an animal from cytotoxic side effects of the administration of a mitotic phase cell cycle inhibitor or a topoisomerase inhibitor comprising administering to the animal, in advance of administration of said inhibitor, an effective amount of at least one cytoprotective aryl or heteroaryl propene amide of formula I^{ii}:



I^{ii}

wherein:

ring A and ring B are independently selected from the group consisting of aryl and heteroaryl;

X is O or S;

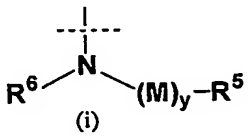
R^1 is independently selected from the group consisting of $-R^4$, $-SO_2(C_1-C_6)$alkyl, $-C(=O)R^4$, $-C(=O)OR^4$, $-C(=O)O(C_1-C_6)$alkylenearyl, $-OR^4$, $-(C_2-C_6)$alkynyl, $-(C_3-C_6)$heteroalkenyl, $-(C_2-C_6)$alkylene-OR^4, substituted aryl, unsubstituted aryl, substituted heteroaryl, unsubstituted heteroaryl, substituted aryl(C_1-C_3)alkyl, unsubstituted aryl(C_1-C_3)alkyl, substituted heteroaryl(C_1-C_3)alkyl and unsubstituted heteroaryl(C_1-C_3)alkyl;

R^2 is independently selected from $-(C_1-C_6)$alkyl, halogen, $-OR^4$, $-C\equiv N$, $-NO_2$, $-CO_2R^4$, $-C(=O)NR^4{}_2$, $-C(=NR^4)NR^4{}_2$, $-O(C_1-C_3)$alkylene-CO_2R^4, $-(C_2-C_6)-OR^4$, phosphonato, $-NR^4{}_2$, $-NHC(=O)(C_1-C_6)$alkyl, sulfamyl, carbamyl, $-OC(=O)(C_1-C_3)$alkyl, $-O(C_2-C_6)-N((C_1-C_6)\text{alkyl})_2$, $-S(C_1-C_3)$alkyl, $-S(=O)(C_1-C_3)$alkyl $-(C_1-C_3)$perfluoroalkyl and $-SO_2(C_1-C_3)$alkyl;

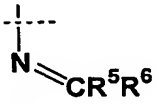
b is 1, 2, 3, 4 or 5;

∿∿∿ indicates a single bond, whereby the compounds of formula I may be in either the E or the Z conformation;

R^3 is independently selected from halogen, -(C_1-C_6)alkyl, -OR^4 -C≡N, -C(=O)NR^4_2, -C(=O)OR^4, -C(=NR^4)NR^4_2, –O(C_1-C_3)alkylene-CO_2R^4, -(C_1-C_6)-OR^4, nitro, phosphonato, -NHC(=O)(C_1-C_6)alkyl, sulfamyl, carbamyl, -OC(=O)(C_1-C_3)alkyl, -O(C_2-C_6)-N((C_1-C_6)alkyl)$_2$, -(C_1-C_3)perfluoroalkyl and (i) or (ii) below:



(i)



(ii)

wherein:

each M is a bivalent connecting group independently selected from the group consisting of –(C_1-C_6)alkylene–, –(CH_2)$_d$-V-(CH_2)$_e$–, –(CH_2)$_f$-W-(CH_2)$_g$– and –Z–;

each y is independently selected from the group consisting of 0 and 1;

each V is independently selected from the group consisting of arylene, heteroarylene, -C(=O)-, -C(=O)(C_1-C_6)perfluoroalkylene, –C(=O)–, –C(=S)–, –S(=O)–, –SO_2–, –C(=O)NR^4–, –C(=S)NR^4– and –SO_2NR^4–;

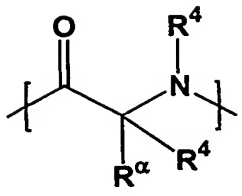
each W is independently selected from the group consisting of –NR^4–, –O– and -S–;

each d is independently selected from the group consisting of 0, 1 and 2;

each e is independently selected from the group consisting of 0, 1 and 2;

each f is independently selected from the group consisting of 1, 2 and 3;

each g is independently selected from the group consisting of 0, 1 and 2;

-Z- is  ;

wherein the absolute stereochemistry of –Z– is S or R, or a mixture of S and R;

each R^{α} is independently selected from the group consisting of -H, -(C_1-C_6)alkyl, -$(CH_2)_3$-NH-C(NH_2)(=NH), -CH_2C(=O)NH_2, -CH_2COOH, -CH_2SH, -$(CH_2)_2$C(=O)-NH_2, -$(CH_2)_2$COOH, -CH_2-(2-imidazolyl), -$(CH_2)_4$-NH_2, -$(CH_2)_2$-S-CH_3, phenyl, CH_2-phenyl, -CH_2-OH, -CH(OH)-CH_3, -CH_2-(3-indolyl), -CH_2-(4-hydroxyphenyl); and includes compounds wherein R^{α} and R^4 combine to form a 5-, 6- or 7-membered heterocyclic or carbocyclic ring;

a is 1, 2 or 3;

R^4 is independently selected from the group consisting of –H, -(C_1-C_6)alkyl, substituted -(C_1-C_6)alkyl, -(C_2-C_6)alkenyl, substituted -(C_2-C_6)alkenyl and heteroalkyl, wherein two R^4 groups may together form a heterocycle;

each R^5 is independently selected from the group consisting of -R^4, unsubstituted aryl, substituted aryl, substituted heterocyclic, unsubstituted heterocyclic, -CO_2R^4, -C(=O)NR^4_2, -C(=NH)-NR^4_2, -(C_1-C_6)perfluoroalkyl, -CF_2Cl, -P(=O)(OR^4)$_2$, -OP(=O)(OR^4)$_2$, -$CR^4R^7R^8$ and a monovalent peptidyl moiety with a molecular weight of less than 1000; provided that when y is 0 and R^5 is –CO_2R^4; then R^4 is not –H;

each R^6 is independently selected from the group consisting of –H, -(C_1-C_6)alkyl, and aryl(C_1-C_3)alkyl;

each R^7 is independently selected from the group consisting of –H, -(C_1-C_6)alkyl, –C(=O)R^8, -OR^4, -SR^4, -OC(=O)$(CH_2)_2CO_2R^6$, guanidino, -NR^4_2, -$NR^4_3{}^+$, -$N^+(CH_2CH_2OR^5)_3$, halogen, phenyl, substituted phenyl, heterocyclyl, and substituted heterocyclyl; and

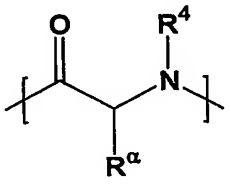
each R^8 is independently selected from the group consisting of R^{α}, halogen, -NR^4_2 and heterocycles containing two nitrogen atoms;

wherein the substituents for the substituted aryl and substituted heterocyclic groups comprising or included within Ar, R^1, R^5 R^6, R^7 and R^α are independently selected from the group consisting of halogen, -(C_1-C_6)alkyl, -(C_1-C_6)alkoxy, -NO_2, -C≡N, -C(=O)O(C_1-C_3)alkyl, -OR^4, -(C_2-C_6)-OR^4, phosphonato, -NR^4_2, -NHC(=O)(C_1-C_6)alkyl, sulfamyl, carbamyl, -OC(=O)(C_1-C_3)alkyl, -O(C_2-C_6)-N((C_1-C_6)alkyl)$_2$ and -(C_1-C_3)perfluoroalkyl; or a salt of such a compound;

wherein the mitotic phase cell cycle inhibitor or topoisomerase inhibitor is not a compound of formula I^{ii}.

69. The method according to claim 68,

wherein, -Z- is:



;

wherein the absolute stereochemistry of –Z– is either S or R; and

each R^α is independently selected from the group consisting of -H, -CH_3, -(CH_2)$_3$-NH-C(NH_2)(=NH), -CH_2C(=O)NH_2, -CH_2COOH, -CH_2SH, -(CH_2)$_2$C(=O)-NH_2, -(CH_2)$_2$COOH, -CH_2-(2-imidazolyl), -CH(CH_3)-CH_2CH_3, -CH_2CH(CH_3)$_2$, -(CH_2)$_4$-NH_2, -(CH_2)$_2$-S-CH_3, phenyl, CH_2-phenyl, -CH_2-OH, -CH(OH)-CH_3, -CH_2-(3-indolyl), -CH_2-(4-hydroxyphenyl), -CH(CH_3)$_2$ and –CH_2CH_3; and includes compounds wherein R^α and R^4 combine to form a 5-, 6- or 7-membered heterocyclic ring;

b is 1, 2 or 3;

each R^7 is independently selected from the group consisting of –H, -(C_1-C_6)alkyl and -(C_1-C_6)acyl;

each V is independently selected from the group consisting of –C(=O)–, –C(=S)–, –S(=O)–, –SO_2–, –C(=O)NR^4–, –C(=S)NR^4– and –SO_2NR^4–;

each R^5 is independently selected from the group consisting of -R^4, unsubstituted aryl, substituted aryl, substituted heterocyclic, unsubstituted

heterocyclic, $-CO_2R^4$, $-C(=O)NR^4_2$, $-C(=NH)-NR^4_2$, and a monovalent peptidyl moiety with a molecular weight of less than 1000; provided that when y is 0 and R^5 is $-CO_2R^4$; then R^4 is not –H; and

wherein the substituents for the substituted aryl and substituted heterocyclic groups comprising or included within Ar, R^1, R^5 and R^α are independently selected from the group consisting of halogen, $-(C_1-C_6)$alkyl, $-(C_1-C_6)$alkoxy, $-NO_2$, $-C\equiv N$, $-C(=O)O(C_1-C_3)$alkyl, $-OR^4$, $-(C_2-C_6)-OR^4$, phosphonato, $-NR^4_2$, $-NHC(=O)(C_1-C_6)$alkyl, sulfamyl, carbamyl, $-OC(=O)(C_1-C_3)$alkyl, $-O(C_2-C_6)-N((C_1-C_6)\text{alkyl})_2$ and $-(C_1-C_3)$perfluoroalkyl; or a salt of such a compound.

70. The method according to claim 68 wherein the mitotic phase cell cycle inhibitor is selected from the group consisting of vinca alkaloids, taxanes, naturally occurring macrolides, and colchicine and its derivatives.

71. The method according to claim 70 wherein the mitotic phase cell cycle inhibitor is selected from the group consisting of paclitaxel and vincristine.

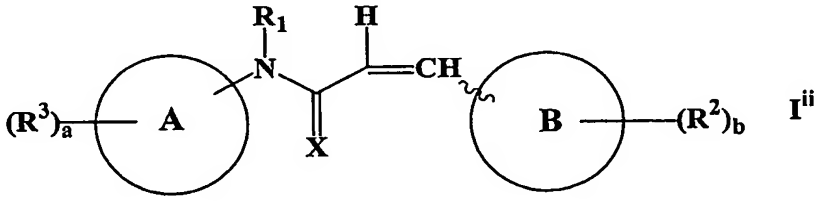
72. The method according to claim 68 wherein the topoisomerase inhibitor is selected from the group consisting of camptothecin, etoposide and mitoxantrone.

73. The method according to claim 68 wherein the cytoprotective compound is administered at least about 4 hours before administration of the mitotic phase cell cycle inhibitor or topoisomerase inhibitor.

74. The method according to claim 73 wherein the cytoprotective compound is administered at least about 12 hours before administration of the mitotic phase cell cycle inhibitor or topoisomerase inhibitor.

75. The method according to claim 74 wherein the cytoprotective compound is administered at least about 24 hours before administration of the mitotic phase cell cycle inhibitor or topoisomerase inhibitor.

76. A method for treating cancer or other proliferative disorder comprising administering to an animal an effective amount at least one cytoprotective compound of formula I^{ii}:



I^{ii}

wherein:

ring A and ring B are independently selected from the group consisting of aryl and heteroaryl;

X is O or S;

R^1 is independently selected from the group consisting of $-R^4$, $-SO_2(C_1-C_6)$alkyl, $-C(=O)R^4$, $-C(=O)OR^4$, $-C(=O)O(C_1-C_6)$alkylenearyl, $-OR^4$, $-(C_2-C_6)$alkynyl, $-(C_3-C_6)$heteroalkenyl, $-(C_2-C_6)$alkylene-OR^4, substituted aryl, unsubstituted aryl, substituted heteroaryl, unsubstituted heteroaryl, substituted aryl(C_1-C_3)alkyl, unsubstituted aryl(C_1-C_3)alkyl, substituted heteroaryl(C_1-C_3)alkyl and unsubstituted heteroaryl(C_1-C_3)alkyl;

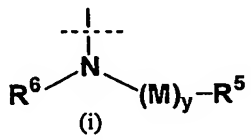
R^2 is independently selected from $-(C_1-C_6)$alkyl, halogen, $-OR^4$, $-C\equiv N$, $-NO_2$, $-CO_2R^4$, $-C(=O)NR^4{}_2$, $-C(=NR^4)NR^4{}_2$, $-O(C_1-C_3)$alkylene-CO_2R^4, $-(C_2-C_6)-OR^4$, phosphonato, $-NR^4{}_2$, $-NHC(=O)(C_1-C_6)$alkyl, sulfamyl, carbamyl, $-OC(=O)(C_1-C_3)$alkyl, $-O(C_2-C_6)-N((C_1-C_6)\text{alkyl})_2$, $-S(C_1-C_3)$alkyl, $-S(=O)(C_1-C_3)$alkyl $-(C_1-C_3)$perfluoroalkyl and $-SO_2(C_1-C_3)$alkyl;

b is 1, 2, 3, 4 or 5;

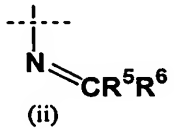
∿∿∿ indicates a single bond, whereby the compounds of formula I may be in either the E or the Z conformation;

R^3 is independently selected from halogen, $-(C_1-C_6)$alkyl, $-OR^4$ $-C\equiv N$, $-C(=O)NR^4{}_2$, $-C(=O)OR^4$, $-C(=NR^4)NR^4{}_2$, $-O(C_1-C_3)$alkylene-CO_2R^4, $-(C_1-C_6)-$

OR^4, nitro, phosphonato, -NHC(=O)(C_1-C_6)alkyl, sulfamyl, carbamyl, -OC(=O)(C_1-C_3)alkyl, -O(C_2-C_6)-N((C_1-C_6)alkyl)$_2$, -(C_1-C_3)perfluoroalkyl and (i) or (ii) below:



(i)



(ii)

wherein:

each M is a bivalent connecting group independently selected from the group consisting of –(C_1-C_6)alkylene–, –$(CH_2)_d$-V-$(CH_2)_e$–, –$(CH_2)_f$-W-$(CH_2)_g$– and –Z–;

each y is independently selected from the group consisting of 0 and 1;

each V is independently selected from the group consisting of arylene, heteroarylene, -C(=O)-, -C(=O)(C_1-C_6)perfluoroalkylene, –C(=O)–, –C(=S)–, –S(=O)–, –SO_2–, –C(=O)NR^4–, –C(=S)NR^4– and –SO_2NR^4–;

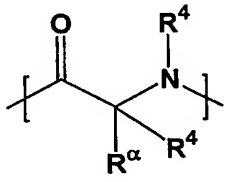
each W is independently selected from the group consisting of –NR^4–, –O– and -S–;

each d is independently selected from the group consisting of 0, 1 and 2;

each e is independently selected from the group consisting of 0, 1 and 2;

each f is independently selected from the group consisting of 1, 2 and 3;

each g is independently selected from the group consisting of 0, 1 and 2;

-Z- is  ;

wherein the absolute stereochemistry of –Z– is S or R, or a mixture of S and R;

each R^{α} is independently selected from the group consisting of -H, -(C_1-C_6)alkyl, -$(CH_2)_3$-NH-C(NH_2)(=NH), -CH_2C(=O)NH_2, -CH_2COOH, -CH_2SH, -$(CH_2)_2C$(=O)-NH_2, -$(CH_2)_2COOH$, -CH_2-(2-imidazolyl), -$(CH_2)_4$-NH_2, -$(CH_2)_2$-S-CH_3, phenyl, CH_2-phenyl, -CH_2-OH, -CH(OH)-CH_3, -CH_2-(3-indolyl), -CH_2-(4-hydroxyphenyl); and includes compounds wherein R^{α} and R^4 combine to form a 5-, 6- or 7-membered heterocyclic or carbocyclic ring;

a is 1, 2 or 3;

R^4 is independently selected from the group consisting of –H, -(C_1-C_6)alkyl, substituted -(C_1-C_6)alkyl, -(C_2-C_6)alkenyl, substituted -(C_2-C_6)alkenyl and heteroalkyl, wherein two R^4 groups may together form a heterocycle;

each R^5 is independently selected from the group consisting of -R^4, unsubstituted aryl, substituted aryl, substituted heterocyclic, unsubstituted heterocyclic, -CO_2R^4, -C(=O)NR^4_2, -C(=NH)-NR^4_2, -(C_1-C_6)perfluoroalkyl, -CF_2Cl, -P(=O)$(OR^4)_2$, -OP(=O)$(OR^4)_2$, -$CR^4R^7R^8$ and a monovalent peptidyl moiety with a molecular weight of less than 1000; provided that when y is 0 and R^5 is –CO_2R^4; then R^4 is not –H;

each R^6 is independently selected from the group consisting of –H, -(C_1-C_6)alkyl, and aryl(C_1-C_3)alkyl;

each R^7 is independently selected from the group consisting of –H, -(C_1-C_6)alkyl, –C(=O)R^8, -OR^4, -SR^4, -OC(=O)$(CH_2)_2CO_2R^6$, guanidino, -NR^4_2, -$NR^4_3{}^+$, -$N^+(CH_2CH_2OR^5)_3$, halogen, phenyl, substituted phenyl, heterocyclyl, and substituted heterocyclyl; and

each R^8 is independently selected from the group consisting of R^{α}, halogen, -NR^4_2 and heterocycles containing two nitrogen atoms;

wherein the substituents for the substituted aryl and substituted heterocyclic groups comprising or included within Ar, R^1, R^5 R^6, R^7 and R^{α} are independently selected from the group consisting of halogen, -(C_1-C_6)alkyl, -(C_1-C_6)alkoxy, -NO_2, -C≡N, -C(=O)O(C_1-C_3)alkyl, -OR^4, -(C_2-C_6)-OR^4, phosphonato, -NR^4_2, -NHC(=O)(C_1-C_6)alkyl, sulfamyl, carbamyl, -OC(=O)(C_1-

C_3)alkyl, -O(C_2-C_6)-N((C_1-C_6)alkyl)$_2$ and -(C_1-C_3)perfluoroalkyl; or a salt of such a compound;

followed by an effective amount of at least one mitotic phase cell cycle inhibitor or topoisomerase inhibitor after administration of the cytoprotective compound.

77. The method according to claim 76 wherein the mitotic phase cell cycle inhibitor is selected from the group consisting of vinca alkaloids, taxanes, naturally occurring macrolides, and colchicine and its derivatives.

78. The method according to claim 77 wherein the mitotic phase cell cycle inhibitor is selected from the group consisting of paclitaxel and vincristine.

79. The method according to claim 76 wherein the topoisomerase inhibitor is selected from the group consisting of camptothecin, etoposide and mitoxantrone.

80. The method according to claim 76 wherein the cytoprotective compound is administered at least about 4 hours before administration of the mitotic phase cell cycle inhibitor or topoisomerase inhibitor.

81. The method according to claim 80 wherein the cytoprotective compound is administered at least about 12 hours before administration of the mitotic phase cell cycle inhibitor or topoisomerase inhibitor.

82. The method according to claim 81 wherein the cytoprotective compound is administered at least about 24 hours before administration of the mitotic phase cell cycle inhibitor or topoisomerase inhibitor.